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FRACTURES RESULTING FROM ECLAMPTIC CONVULSIONS

Review of Literature, Case Reports, and Medicolegal Implications

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THE purpose of this paper is threefold: first, to give a résumé of the literature pertaining to this subject; second, to report our own case and conclusions; third, to mention and to stress the medicolegal aspects of this condition.

In review of the available world literature, eight cases of fractures resulting from eclamptic convulsions were found. These fractures are chiefly of the long bones and of the vertebral column. The upper one-third of the humerus is most frequently involved in the long bones and the vertebral bodies of the thoracic vertebrae are the most frequent sites of fractures in the vertebral column. These are nearly always compression fractures of the bodies, and are identical to those reported due to convulsions caused by electroshock therapy. Most cases of compression fractures due to eclamptic convulsions are not recognized while the patient is in the hospital. After discharge, she continues to have backache or back symptoms for a long period of time, and, if x-rays are taken, they reveal an old compression fracture of the vertebral body. The fractures of the long bones are more symptomatic, and consequently can be diagnosed before discharge from the hospital. These fractures are extremely rare, but should be thought of in every case of eclampsia. The suggestion is offered that x-rays to rule out fractures should be routine procedure in all cases of eclampsia.

Case Report

Mrs. H. M. L., aged 27 years, gravida i, para i, was first seen in the thirty-sixth week of gestation. The routine prenatal examination and the prenatal course were normal. The weight gain was 22 pounds, blood pressure averaged 120/80, and the urine was negative. She went spontaneously into normal labor at the forty-first week of gestation. On her

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admission to the labor room, the blood pressure was 156/100, and the urine was negative. Uterine contractions were occurring every two to three minutes, and were hard. Demerol and scopolamine analgesia were given. After a short labor, during which the highest blood pressure reading was 140/84, the patient was delivered under cyclopropane anesthesia, with low forceps and a left mediolateral episiotomy, of a normal living female child. The estimated blood loss was 300 c.c. The patient was left on the delivery table for one hour as is routine, and the uterus was well contracted when she was moved to her room. About two hours later, the attending nurse called to notify us that the patient was having a convulsion. Before we could arrive at the hospital, she had another convulsion. Sedation was given immediately with resulting control of the convulsion. Only these two convulsions occurred. The blood pressure was 158/70. During the next twenty-four hours, the patient complained of backache and pain in the left shoulder. This pain did not lessen, and an orthopedic specialist was consulted. X-rays ordered by him revealed a fracture of the anatomical neck of the humerus, and slight compression of the body of the eighth thoracic vertebra. The orthopedist then took over care of the fractures. Her postpartum course was otherwise normal and the patient was discharged from the hospital on the ninth postpartum day.

She then instituted suit for neglect, charging that the eclamptic convulsions and fractures should have been prevented by proper medical supervision. Judgment was rendered against the defendant, but was reversed and thrown out in a higher court. Eclampsia cannot be prevented in certain cases, and this case certainly offered no symptoms or indications that postpartum eclampsia would occur.

Questionnaires were sent to seventy medical schools in the United States asking the following questions of their obstetrical departments:

1. Have you had any cases of fractures (spine, long bones, hip, shoulder, etc.), due to eclamptic convulsions?
2. If "Yes" to above, how many cases?
3. Were these cases reported in the literature?
4. How many cases of eclampsia have you had on your service (ten-year survey, etc.)?
5. If possible, please attach hereto a brief résumé of your case, or cases.

Replies to thirty-nine of these questionnaires were received. The totals were as follows:

1. Fractures due to eclamptic convulsions not reported in literature	2
2. Dislocations of jaw	2
3. Total cases of eclampsia (approximately)	1,479

We can draw the conclusion from the handling of at least 1,479 cases of eclampsia in ten years by these thirty-nine medical schools that this condition is rare, but that it does occur. Also, we must remember that in the last ten years the incidence of eclampsia has been greatly reduced, mainly through better prenatal care. Many medical schools reported only one or two cases of eclampsia every year.

Abstracts of Cases in the World Literature

CASE 1.—A. D. F. was 42 years of age, gravida vii, para vi. All pregnancies were normal. The past history was not contributory. The present pregnancy was not remarkable until the last month, when she noticed edema of the lower limbs, more intense and diffuse than with any of the previous pregnancies. Urinalysis showed a small amount of albumin.

The day following normal parturition, the patient had tonic-clonic convulsions. These convulsions lasted two to three minutes, and occurred four times in the same day. Early the following morning she had a most violent and intense attack, with involuntary emission of urine and feces, lasting two or three minutes. She then became quiet and unconscious and fell prostrate, later complaining of a violent pain in the right hip. The pain was so acute and so spontaneous that it increased in severity whenever she attempted to change her position. Moreover, she noticed a swelling of the entire region of the hip. She remained in bed thirty days. Then, since the swelling had disappeared and the pain was much improved, she began to get up and to move cautiously about, helping herself with a support. In her walk, she always favored the right hip as much as possible. After two years, not having recovered, she presented herself for observation. Physical examination was essentially noncontributory with the exception of the right side. She definitely walked with a limping gait favoring the right side, and in walking she supported herself with a solid cane. The lower right limb was externally rotated and abducted, and was shortened 5 cm. It was further noted that the elevation of the greater trochanter was slightly evident on the right side and that it was raised in comparison with the left. Radiological examination of the right hip clearly demonstrated that there was a fracture of the acetabulum, and that the head and neck of the femur had penetrated into the small pelvis where a second joint had been formed. The crushing in of the acetabulum, and the accompanying luxation of the head of the femur within the pelvis were brought about in the last seizure of eclampsia suffered by the patient two days after parturition. According to the members of the family, the eclamptic convulsions were particularly violent and disorderly. The contractions pulled the heavy femur against the acetabulum with the resulting fracture of the socket and penetration of the head and neck of the femur into the small pelvis. The damage to the patient from this injury was limited exclusively to her lameness. No therapy can bring about anything useful to the articulation.

CASE 2.—M., aged 28, gravida ii, para ii, was delivered of her first child seven years previously without disturbances. The second normal delivery occurred on June 25, 1932, at 11 P.M., labor lasting three hours. During the middle of the next day, she suffered two attacks of loss of consciousness in the presence of her husband and her mother and, shortly thereafter, in the presence of the midwife, she suffered a third attack of one minute's duration. During the second half of these three attacks, the patient executed violent pushing movements downward with both arms slightly bent and maximately supinated. Fifty minutes after the third attack, her physician saw the patient who was unconscious. Her face was pale and edematous; there was a very pronounced edema of both lower legs and of the back of the hands. She was transferred to the hospital. The temperature was 36.8° C., pulse 80, blood pressure 160/100. The reflexes were normal. The patient sighed severely when attempt was made to move the right upper arm passively. On June 27 the patient was still rather dazed. Urinalysis showed less albumin; no red blood cells were seen. The reflexes were the same as before. The right upper arm was very painful during motion. External or bone injuries could not be seen. The right arm was placed in abduction between two pillows. On June 28 the patient was again conscious, and was given a diet for eclampsia. Her vision was slightly hazy, the pain in the right upper arm was unchanged. The blood pressure was 180/100, the edema was less. On June 30, neurological examination showed indication of a Babinski reflex of the right side. All other reflexes were normal. Ophthalmoscopic examination showed no pathological findings. X-ray of the right upper arm disclosed an oval-shaped fracture of the tuberculum minus, with little dislocation of the fracture distally. From this star-shaped injury which was near the acetabulum was noticeable a fracture into the inside of this humerus. The upper part of the fracture was slightly elevated and opened up toward the body itself. The fracture was fixed at a 90 degree abduction of the upper arm by extension. The further course was favorable and she was discharged on August 22 in good condition. The fracture of the upper arm was treated further with active exercises, heat, and massage, so that toward the end of October ability to move and use the arm was almost completely restored. X-ray showed a good healing

of the fracture. We dealt, therefore, with the fracture of the upper arm which this woman suffered during the clonic phase of her eclamptic attack. It was ascertained by repeated questioning of the husband, that this woman had never been alone after delivery until she was brought to the hospital. She was accompanied by her husband and well-trained personnel on the transfer to the hospital. In the hospital, the patient was continuously supervised. There had been no fall out of bed, nor any other external injury. She had felt quite well until the beginning of the eclamptic attack, and could use the right arm without any difficulty. With regard to the mechanism of the occurrence of the fracture of the tuberculum minus, it can be said here only that this fracture is extremely rare, and it can be considered as a torsion fracture, particularly during excessive turning of the arm outward.

CASE 3.—This was a case of postpartum eclampsia in which two convulsions occurred. The patient had an anterior dislocation of the left humerus, and an avulsion fracture of the greater tuberosity after the first eclamptic convulsion. This occurred on Dec. 31, 1948.

CASE 4.—Mrs. T. was delivered about Sept. 20, 1948. She developed postpartum eclampsia and had several convulsions. She recovered under treatment and returned home, apparently in good condition. She returned for a postpartum checkup on Oct. 29, 1948, at which time she was complaining of backache, and showed a slight dorsal kyphosis. X-ray examination showed compression fracture of the eighth dorsal vertebra, which was undoubtedly due to eclamptic convulsions. Recovery has been uneventful. Her health, at this time, is excellent.

CASE 5.—M. P., gravida i, para 0, aged 32 years, eight weeks pregnant, was admitted to the hospital unconscious with half-hour eclamptic fits. In spite of the Stroganoff treatment, the attacks ceased only on the third day after induction of labor and delivery. Three and one-half weeks after the patient got up, she complained of slight pain in the back, which ceased two months later. After a further two months, she noticed that she was stooping. Her stoop became steadily worse and, at the same time, her back began to ache in the dorsal region, especially after housework. The pain ceased if she lay down on a hard couch with her back straight. The patient was of medium size, asthenic in build, with a decided stoop. On examination, she was found to have an accentuated kyphosis of the upper and middle dorsal spine, evenly distributed. The erector spinae muscles appeared bulky, and stretched on both sides. The spinal processes of the fourth, fifth, and sixth dorsal vertebrae were tender. There were excessive lumbar lordosis and decreased mobility of the spine. X-rays taken four months after delivery showed that the fourth, fifth, and sixth dorsal vertebrae were slightly wedge shaped, with trapezoid flattening. The end-plates appeared crossed, especially anteriorly, where the bone was irrgularly thickened. The intervertebral spaces were slightly narrowed anteriorly. The dorsal kyphosis was marked with compensatory lordosis of the lumbar region.

CASE 6.—S. K., gravida ii, para i, 24 years of age, was admitted with albuminuria and edema, followed by eclamptic fits every half-hour. She was delivered by cesarean section and the convulsions subsided slowly. Four weeks later, the patient noticed that her back felt stiff when she started to walk. She tired easily, and the pain in the back radiated to the abdomen. The family observed that she had begun to stoop. On examination, the physiological curve of the spine (both dorsal kyphosis, and lumbar lordosis) was seen to be accentuated. The spinal processes of the sixth and seventh dorsal vertebrae were tender, and dorsal motility was reduced. X-ray showed that the bodies of the fourth to eighth dorsal vertebrae were flattened anteriorly—the sixth and seventh were wedge shaped—and the ninth had an insignificant oblique line through the upper end-plate. All the end-plates, except the lower end-plate of the ninth, were abnormally dense, together with the joining parts of the vertebral bodies. The bone structure was blurred. There was a slight narrowing of the anterior part of the intervertebral space between the sixth and seventh dorsal vertebrae. Kyphosis of the dorsal region was marked, with protrusion of the sixth and seventh vertebrae.[5]

Treatment of Cases 5 and 6.—Both of these patients were treated with hyperextension and plaster of Paris with physical exercises. When the plaster was removed after twelve weeks,

the first patient showed only slightly improved posture; the second considerable improvement. They now wear only a linen corset for support, and during the whole period of observation have been free from pain.

CASE 7.—R. M., gravida i, para 0, 18 years old, had always been in good health, but four days before admission she felt very ill, with edema and albuminuria. On admission, clonic convulsions occurred, each lasting about two minutes. As the attacks became worse, and in view of her general condition, cesarean section was performed, and a live child was delivered. Three hours after operation, convulsive attacks recurred. Lumbar puncture did not show increased pressure in the cerebral spinal fluid. The attacks continued and the patient died eight hours after operation. Postpartum examination showed only slight change in the internal organs. The cartilage of the first lumbar vertebra was torn, and the upper end-plates were fractured irregularly. The intervertebral disc between the twelfth thoracic and first lumbar vertebrae was prolapsed. Histological examination showed a large zone of fibrous transformation of the marrow in the first lumbar vertebra, with secondary cartilage formation and increased vascularity. X-rays confirmed that there was a compression fracture of the first vertebra with traumatic prolapse of the intervertebral disc.[5]

Comment

"The vertebral column protects the spinal cord, and its snakelike curve is important because it enables it to take without damage a far greater strain than a straight column support. The muscles which influence flexion and extension of the vertebral column are coordinated. All extensors, with few exceptions, bend the spine backward, but are weaker in the dorsal region than in the lumbar and cervical (Fick). The flexors form a muscle chain from sternomastoid, which bends the head, to iliopsoas, which increases the lumbar lordosis. Mobility in the dorsal region is limited to ninety degrees of flexion and to forty degrees of extension, so that the flexors gain a mechanical advantage. This may explain the changes in the anterior part of the vertebrae after convulsions. Then abruptness of the strain on the vertebrae is an important factor as the margin of elasticity is exceeded with relatively little applied force, especially when, as in convulsions, blow succeeds blow in quick succession. Every blow will deform a vertebrae already made rigid by force which has exceeded the limit of elasticity, and the result can only be a fracture. This may be a major fracture, or merely a crushed trabecula. In the latter case, a low sinking of the vertebral body will result with increasing kyphosis. The anterior part of the affected vertebrae is flattened, leaving them wedge-shaped, or trapezoid, and the end-plates are thickened together with the spongiosa of the vertebral body which becomes irregularly dense, especially anteriorly.

"It has been mentioned that in pregnancy, decalcification of the pelvis in particular (and less extensive decalcification of other bones of the body) may lead to predisposition to fracture from convulsions during pregnancy. However, not enough cases have been studied or followed to draw any definite conclusions. X-rays taken of these cases show no abnormal decalcification, and this assumption is merely theoretical.

"Differential diagnosis (only the commoner conditions are mentioned): 1. Deformity due to convulsion therapy, or tetanus. Similar to post-eclamptic convulsions. 2. Adolescent dorsal kyphosis. Located lower in the dorsal section with the center of deformity in the eighth and ninth vertebral bodies.

Changes are also found in the vertebral disc (node of Schmorl). 3. Senile kyphosis. Enlargement of intervertebral spaces and fishlike vertebrae. 4. Osteomalacia. General clinical symptoms. Atrophy of vertebral bodies. Enlargement of intervertebral space. 5. Spinal tuberculosis. Stiffness of the affected part of the spine and later gibbous. Irregular intervertebral spaces. Cold abscesses.''[5]

It is suggested that the fractures in the cases described here, due to abrupt and recurring muscle contractions acting on the bones, exceed the limit of elasticity, and finally cause a split of the trabeculae with an accentuated dorsal kyphosis, or fracture proper. Fractures of the humerus are thought to be caused by overaccentuation of external rotation. From the therapeutic point of view, we recommend complete radiological examination of any individual who has had eclamptic convulsions before leaving the hospital, and repetition of this after four weeks, if any symptoms are presented by the patient which would indicate that some compression of the vertebra or a ruptured intervertebral disc had occurred.

One very important consideration in any of these cases is the possibility of external violence, i.e., falling off the delivery table, or out of bed, or some other form of accident occurring to the patient before or after delivery. In all of the cases here presented there was no evidence that any such injury occurred. The only conclusion that can be drawn in these cases is that the injuries are the direct result of eclamptic convulsions.

We feel that the medicolegal aspect of this condition is of major importance. The patient in our case instituted suit for neglect in that the eclamptic convulsions and resultant fracture should have been prevented by proper medical supervision. One of the primary contentions in the litigation was the statement made in a textbook, *The Toxemias of Pregnancy*,[6] that all cases of eclampsia could be prevented by proper medical supervision. This was a very unfortunate statement to be made so positively, and has since been retracted in other articles by the author. It must be kept in mind that all patients who come to an obstetrician in the last month of pregnancy have been under the care of another physician, and have left his care for some reason, usually either financial or because of noncooperation with him. These patients present themselves to their new doctor in the last month of pregnancy, and many, although they give a history of a normal weight gain and no apparent symptoms of toxemia, are incipiently toxic. Since the occurrence of this case, we have made it a point to watch patients of this type who come to us in the last month of pregnancy, and it has been amazing to note the symptoms they conceal pertaining to toxemia, particularly hidden weight gain. We therefore recommend that all patients who first appear for prenatal care in the last month of pregnancy should be watched more closely than any other type of patient.

Judgment was rendered against the defendent in the lower courts, but was reversed and thrown out in the higher courts, the reason being that sufficient evidence had not been presented in the original trial to substantiate the findings that any neglect or mismanagement of the case had occurred. If the judg-

ment in this case had been upheld, its significance would have been far reaching, in that the medical profession would be held responsible for any complications or any bad results that occur in any disease for any reason whatsoever. In other words, the responsibility for all bad results and all complications would be placed on the medical profession. In contrast, at present, if a doctor is practicing medicine as accepted in his home community to the best of his ability, no criticism can be offered as to complications and bad results. The trial in this case also bears out the serious results that dogmatic statements in medical textbooks may lead to. Writers of medical texts should be very careful about making positive statements, as the legal profession's main source of information in medicolegal suits is from these medical textbooks which are accepted as authoritative in courts of law.

Conclusions

1. Eclamptic convulsions cause fractures which are similar to those found after convulsive therapy.

2. These fractures are most common in cases of postpartum eclampsia and are chiefly those of the long bones and of the vertebral column.

3. All patients who have had eclamptic convulsions should have a complete radiological examination before leaving the hospital, to be repeated in four weeks if any symptoms compatible with bone injury appear.

4. For medicolegal protection, this x-ray examination should be carried out before discharge from the hospital.

5. All dogmatic statements should be very carefully thought out before final incorporation in a medical textbook.

6. All pregnant patients who present themselves to the obstetrician in the last four weeks of gestation should have much more careful supervision on account of possible concealed toxemia, especially concealed weight gain, which might result in eclamptic convulsions, and thereby give rise to medicolegal disputes.

7. It is evident from the sometimes erroneously stated normal weight gain, that, when there is any question of the patient's weight, she should be placed on a detoxifying regimen prior to labor.

8. We have described one of the rarest and least known complications resulting from eclampsia.

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FETAL MORTALITY IN CESAREAN SECTION*

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IN THE past several years, it has become increasingly evident, both in the literature[1, 2] and in our clinical observations, that the decreasing fetal and maternal mortality associated with cesarean section has broadened the indications for section. This changing concept is aptly expressed by McLean,[1] who states, "Earlier intervention, instead of hopeful procrastination, will result in lowered maternal and fetal mortality." The reasons for this increased safety generally are not controversial. They include the sulfonamides, the antibiotics, availability of blood replacement, better prenatal care, and increased availability of operative skill. In addition, much careful work has been done in evaluating the death of the infant born by cesarean section.[3, 4, 5] With the care now being given to the baby born by elective cesarean section its early life is no more hazardous than that following a normal delivery. Kistner,[6] in a ten-year study at the Cincinnati General Hospital, has shown that the fetal mortality following cesarean section was only one-third that following midforceps, and that there has been an over-all diminution in the fetal mortality rate as their cesarean section rate has increased.

At West Suburban Hospital we have maintained a section rate of 3.6 per cent over the last ten years. In the light of present cesarean section safety, are we not justified in relaxing the criteria for section? Cesarean section need not now be considered the last resort, but rather another method of delivery that in many cases will offer more safety to mother and infant. Our fetal and maternal mortailty rates are lower with elective cesarean procedures than with normal delivery. How then can we logically explain an outdated hesitancy to "subject a patient to cesarean section"?

Material

Our series at West Suburban Hospital, an entirely private institution, covers a period from January, 1943, to December, 1952. During this ten-year period, there were 31,393 deliveries, of which 1,131 (3.6 per cent) were sections. There were 880 low cervical (76 per cent), 233 classical (20.5 per cent), 15 cesarean hysterectomies (1.2 per cent), and 3 extraperitoneal sections (0.3 per cent). Most of the classical sections were done during the first five-year period by men who elected that method as the procedure of choice. Most of the operations during the last few years have been of the low cervical type. The majority of cesarean hysterectomies were done by two men who often elect this method to sterilize the patient after the third section. The three extraperitoneal sections were done for teaching purposes. About 95 per cent

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of the sections were performed under inhalation anesthesia, with atropine, 1/150 grain, the only preoperative medication. The rest were done under local anesthesia. Spinal anesthesia was employed in only 2 cases during the ten-year period.

In an attempt to compare more fairly the two routes of delivery, we will compare vaginal delivery from 36 weeks on with the elective section.

The slight increase in the percentage of cesarean sections during the latter portion of the ten-year period does not appear to be greatly significant. In this small increase, however, may be included a few cases that otherwise would have had a less satisfactory ending. This may be only a small factor in the decreasing maternal death rate over the period. A substantial part of the increased section rate is on the basis of repeat sections.

TABLE I. TOTAL NUMBER OF DELIVERIES AND SECTIONS FOR TEN YEARS

YEAR	DELIVERIES	SECTIONS	
		NO.	PER CENT
1943	2,528	69	2.3
1944	2,357	66	2.8
1945	2,390	74	3.1
1946	3,188	113	3.5
1947	3,489	124	3.5
1948	3,333	110	3.3
1949	3,411	130	3.8
1950	3,426	145	4.2
1951	3,590	151	4.2
1952	3,681	149	4.0
Total	31,393	1,131	3.6

Over the ten-year period, repeat sections constituted 40 per cent of the total number of sections. Cephalopelvic disproportion was an indication in only 20 per cent of the cases. These figures are in general disagreement with other large series,[1, 2] where the over-all section rate is higher. In most other series, cephalopelvic disproportion heads the list. The indications for section for the ten-year period are given in Table II.

TABLE II. INDICATIONS FOR CESAREAN SECTION

INDICATION	NUMBER	PER CENT
Previous section	456	40.3
Cephalopelvic disproportion	223	20.0
Abruptio placentae	95	8.4
Placenta previa	86	7.6
Fetal distress	69	6.0
Dysfunctional labor	68	6.0
Nonresponding toxemia	49	4.3
Lack of progress in second stage	48	4.3
Diabetes	10	0.9
Extravaluable baby	8	0.7
Failed forceps	4	0.3
Cardiac	4	0.3
Previous vaginal surgery	4	0.3
Others (one each)	7	0.6
Ventral hernia		
Intrapartum septicemia		
Pyelonephritis		
Previous postpartum psychosis		
Fulminating tuberculosis		
Bowel obstruction		
Existing femoral neck fracture		
Total	1,131	100.0

Prolonged labor may appear conspicuous by its absence. The explanation is that most primigravidas are evaluated with x-ray pelvimetry near term, and there is no fixed duration of labor, which is allowed to continue as long as there is progress, and mother and infant are in good condition.

Of special significance are the 8 extravaluable infants delivered by section. They were all infants of primigravidas, or women who for the first time had carried a gestation to viability. Four of them were elderly; they all had reason to expect this to be their only child. Most of the women had sterility problems of long standing or were habitual aborters. Three were allowed a short trial of labor before elective section. Attention is called to the fact that these patients were electively operated upon by men who may be considered ardent exponents of the lowest possible section rate.

As previously stated, about 97 per cent of the sections were done by obstetrical specialists. They were assisted by a resident and intern or senior medical student. In addition, an obstetrical resident was scrubbed to supervise resuscitation of the newborn. This is standard procedure in our hospital. The baby is taken to a sterile table not ten feet from the operating table, where three sizes of tracheal catheters are available. Whenever spontaneous respirations are delayed, due to narcosis or hypoxia from any cause, adequate oxygenation is maintained with a tracheal catheter and artificial respiration. A special small oxygen system is turned on as the baby is delivered and it receives immediate oxygen for at least 30 minutes or as long as indicated. The trachea is aspirated first with a soft rubber bulb and then, if necessary, with a tracheal catheter. We emphasize prophylaxis in dealing with oxygen deficit, feeling that delay until symptoms appear is frequently attended by more or less irreversible damage to the respiratory center and the cerebral cortex. We have never seen damage to the infant with intratracheal catheterization in skilled hands.

We have eliminated the use of central nervous system stimulants on the newborn. We feel that their benefit is doubtful and they may in some cases be harmful. Why increase the metabolic demand for oxygen and produce more of a relative anoxia when the difficulty is nearly always an obstruction in the airway?

Total Viable Infant Mortality

The total fetal wastage associated with section for all indications and gestation from 28 to 40 weeks, was 69, or 6.1 per cent. This figure includes stillborn and anomalous infants. The causes of death are summarized in Table III.

TABLE III. SECTION INDICATIONS WHERE INFANT WAS STILLBORN OR DIED AFTER DELIVERY

Abruptio placentae	26
Placenta previa	12
Previous section	9
Nonresponding toxemia	8
Cardiac disease	3
Fetal distress	2
Others	9
Acute abdominal crisis with ruptured appendix	
Ruptured uterus	
Intrauterine sepsis	
Pyelonephritis	
Porro operation for fibroids (known stillborn)	
Previous myomectomy (in labor at 33 weeks)	
Cephalopelvic disproportion	
Shoulder presentation (in labor)	
Twins in elderly primipara (one stillborn)	
Total	69

Of the 1,131 sections, a careful analysis of the records shows 678 to be elective and not associated with pathology known before operation. All of these elective sections were performed between 36 weeks and term. The gross fetal wastage for this group was 10, 8 of which were attributed to pathology unrelated to delivery and only 2 of which were without apparent explanation other than the operative procedure, as indicated in Table IV.

TABLE IV. TEN INFANT DEATHS IN 1,131 ELECTIVE SECTIONS

1.	Stillborn at 28 weeks, previous section in labor
2.	Known stillborn at term, previous section in labor
3.	Repeat section at term, congenital atresia of lungs
4.	Previous section in labor, 32 weeks
5.	Erythroblastosis
6.	Hemorrhagic disease of newborn
7.	Erythroblastosis
8.	Marked cephalopelvic disproportion, infant at term but 3 pounds, and very poor placental development
9.	Repeat section, term, unexplained
10.	Repeat section, 38 weeks, atelectasis

Only the last two infant deaths associated with the elective section group cannot be explained on any other basis than the section procedure. This gives a figure of 2 deaths of infants of 36 weeks and over, out of 678 elective procedures, or a fetal death rate of 0.29 per cent for this group. The total fetal wastage for the ten years with cesarean section for all periods and all indications, including stillborn infants was 69, or 6.1 per cent. This figure agrees with those of others,[7, 8] the difference being made up by the cases of early bleeding and the abnormal babies.

In an effort to evaluate accurately cesarean section per se, we must compare the vaginal deliveries with the same reservations taken with the sections; that is, from 36 weeks and on, and attempting to eliminate other causative factors for fetal death. Of the 31,393 deliveries in the ten years, 30,262 were vaginal. A total of 2,058 infants were under 36 weeks, leaving 28,204 infants delivered per vaginam at 36 weeks or over. There was a total of 158 infant deaths, excluding stillbirths, or an uncorrected percentage of 0.56 fetal death rate in vaginal delivery; eliminating the infants with other causes of death gives a figure of 106, or 0.38 per cent. This low figure calculated with near-term infants is not unique with our institution, but rather reflects the tremendous strides of modern obstetrics and scores of very excellent hospitals all over the country.

Table V shows the causes of death in vaginal deliveries from 36 weeks and on, excluding stillbirths.

On the average, our patients are not given heavy sedation. The primiparas receive an average of 250 mg. of Demerol and $\frac{1}{150}$ grain of scopolamine. The multiparas receive an average of 100 mg. of Demerol and $\frac{1}{150}$ grain of scopolamine. At the time of delivery, usually ethylene and oxygen or nitrous oxide is used. Very few of the patients who have vaginal deliveries receive enough gas before the delivery of the baby for it to be a factor in infant mortality from anesthesia. After delivery, they are then anesthetized or given local anesthesia, if it has been elected, and the repair is done. We give only a very occasional spinal anesthetic. The pudendal block is perhaps the favorite of the local analgesic procedures.

As with the babies born by cesarean section, oxygen and tracheal catheters are readily available and the infants are put immediately into heated cribs. This last year, we have not been washing off the infants in the delivery room. Gross blood might be wiped off before the babies are sent to the

nursery, but they receive their first bath not less than 24 hours after delivery. While it is much too early to evaluate this procedure fully, there is the feeling that we are seeing much less rash of the newborn. This may be due to the presence of the vernix for the first 24 hours. Other hospitals have done this for some time past.

TABLE V. CAUSES OF DEATH IN INFANTS OF 36 TO 40 WEEKS FOLLOWING VAGINAL DELIVERY (EXCLUDING STILLBIRTHS)

1. *Anomalies Sufficient to Cause Eventual Death.*— Spina bifida, anencephaly, cardiac abnormality, absence or atresia of organ structures, hydrocephalus, etc.	46
2. *Intrauterine Asphyxia.*— Asphyxia livida, pallida, prolapse of cord, abruptio placentae	37
3. *Not Determined.*— Delayed respirations with inability to resuscitate, sudden death with no abnormal findings, no postmortem	31
4. *Atelectasis.*— Mostly second to fifth day	15
5. *Cerebral Injury.*— Hemorrhage or damage found on postmortem	13
6. *Erythroblastosis*	10
7. *Aspiration Pneumonia*	4
8. *Meningitis.*— Both pneumococcal	2
Total	158

Maternal Mortality

The decrease in maternal mortality during the last decade has been outstanding practically throughout the entire country. Fitzgerald and Webster,[9] in their nineteen-year survey of maternal deaths at the Cook County Hospital, Chicago, showed that the maternal mortality there has dropped from 150 per 10,000 births in 1934 to 7.9 in 1951. This is a particularly remarkable achievement in that the Cook County Hospital receives much varied and unexpected pathology, many of the obstetrical patients being seen for the first time as arrivals in the police ambulance. As they state, "The reasons for the increased safety of motherhood . . . include the sulfonamides, blood banks, the antibiotics, better prenatal care, increased awareness on the part of both physician and patient as to the necessity of prompt investigation of abnormal signs and symptoms." They feel that the greatest hope for the further lowering of the maternal mortality rate lies in the elimination of deaths from toxemia.

At West Suburban Hospital, by far the greatest part of our patients are seen prenatally by private physicians and thus, perhaps, we see fewer neglected cases than charity institutions, with a resulting lower maternal mortality rate. During the ten-year period, however, there has been a marked reduction in our maternal deaths. This reduction is undoubtedly brought about by the factors just mentioned.

In the 10 years, there have been 20 deaths in the obstetrical department, a percentage of 0.067 maternal deaths for the 31,393 deliveries. Five of these deaths were associated in one way or another with cesarean section and in every case were involved with the pathology necessitating the section. Of the 678 elective cesarean sections, there were no maternal deaths.

Table VI shows the maternal death rate for the last ten years.

It is obvious from inspection of Table VII that even with an increased number of deliveries, the maternal death rate has dropped markedly. In addition, the last 4 deaths were not preventable when the patients were seen by the hospital staff. The two patients with abruptio placentae were brought

in by ambulance in severe shock. A section was done on the first one because it was believed that there were still fetal heart tones present, although neither blood pressure nor pulse could be obtained on the mother.

The second patient came in comatose, having convulsions, and no blood pressure or pulse was obtained. Transfusion was started as soon as possible and at section a marginal placenta previa was found. In addition, the placenta was an increta at its lower margins and completely separated above. Estimated blood loss before section was 2,500 c.c. Blood was pumped in under pressure, but the patient did not recover from shock.

TABLE VI. MATERNAL DEATH RATE FOR TEN YEARS

YEAR	DELIVERIES	DEATHS	PER CENT
1943	2,528	5	0.2
1944	2,357	3	0.13
1945	2,390	3	0.125
1946	3,188	5	0.16
1947	3,489	0	0.0
1948	3,333	0	0.0
1949	3,411	1	0.03
1950	3,426	2	0.05
1951	3,590	0	0.0
1952	3,681	1	0.027
Total	31,393	20	0.067

TABLE VII. CAUSES OF MATERNAL DEATHS, 1943 THROUGH 1952

1943.—
1. Previous section with peritonitis, in labor (cesarean)
2. Eclampsia
3. Eclampsia (undelivered)
4. Thrombophlebitis of right ovarian vein
5. Tetanus (patient had been working in field when labor began)

1944.—
1. Multiple liver abscesses found (attempt to save live baby—cesarean)
2. Pulmonary embolism
3. Eclampsia, diabetes mellitus

1945.—
1. Pulmonary embolism
2. Lobar pneumonia
3. Ruptured uterus

1946.—
1. Congenital heart disease, toxemia
2. Ruptured uterus during second stage
3. Pulmonary embolism
4. Chronic nephritis and toxemia
5. Toxemia with anuria

1947.—
No deaths

1948.—
No deaths

1949.—
1. Bilateral cortical and pituitary necrosis, pyelonephritis, and pneumonia

1950.—
1. Abruptio placentae, bled out (cesarean)
2. Acute cardiac failure, comatose (cesarean—attempt to get live baby failed)

1951.—
No deaths

1952.—
1. Abruptio placentae (cesarean effort to get baby)

The patient with heart disease in this last group came in almost in complete heart failure, in labor. It is believed that the patient died just as the section started and the attempt was made to deliver a live baby, but to no avail.

The obstetrical department had delivered 8,261 mothers without a maternal death, until the last death of the patient who arrived in irreversible shock. With the prenatal care most of the patients receive, deaths from toxemia are on the decrease. The patients with severe bleeding, however, arriving at the hospital in such poor condition that even the most heroic efforts are not enough, remain our greatest danger and source of maternal mortality.

Comment

All cesarean sections are reviewed once a month by the obstetrical staff as to their indication and operative results, i.e., condition of baby at time of delivery and the need for resuscitation. All premature and full-term section babies are cared for in a special nursery with trained personnel.

An autopsy is performed by our pathologist and a complete macroscopic and microscopic report is made on all babies that die after section or are stillborn. This gives us an accurate record as to possible causes of fetal deaths.

Under the indications for cesarean section we have listed the "extravaluable baby." We must admit that although this is not exactly a scientific term, its use has crept into the literature in the last few years. While we must recognize that all babies are valuable, we must be cognizant of the fact that mothers who have long been sterile or who are elderly primiparas certainly deserve extra consideration. Our spectrum of the indications for cesarean section in this group should be as broad as possible and we must recognize the apprehension of the mother because of the knowledge that probably this will be her one and only child. Prolonged labor or difficult vaginal delivery may result in a spastic child; therefore, why not consider cesarean section in this case and have as reasonable assurance as possible that she will have a good baby.

Fetal distress is a justifiable indication for section in present-day obstetrics and is a factor in reducing the infant mortality rate as compared to that with the "wait and see" policy of a decade ago.

Repeat cesarean section as an indication is adhered to without exception. Our repeat sections represent 40.3 per cent of total sections. The broadening of the spectrum by this indication is saving many babies. We feel that a repeat section with a competent operator and anesthetist, and the advantages of blood banks, antibiotics, etc., should not carry any higher fetal mortality than vaginal delivery. Our fetal death rate of 0.29 per cent with section, compared to 0.38 per cent in vaginal deliveries without complication, is worthy of consideration.

Summary and Conclusions

1. Our uncorrected maternal death rate at West Suburban Hospital is 0.067 per cent for the ten-year period. This has been further diminished in the last five years.

2. The cesarean section rate is 3.6 per cent and there were no maternal deaths associated with elective cesarean section.

3. The fetal mortality rate with elective cesarean section, from 36 to 40 weeks, excluding stillborn and pathologic infants, is less than for vaginal delivery.

4. Cesarean section per se is safer for the infant than normal vaginal delivery. It is believed, therefore, that a higher section rate would be justified and that the indications for section can be broadened.

5. Premature placental separation now constitutes the greatest danger to mother and infant.

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Discussion

DR. WILLIAM G. CUMMINGS.—I believe there is no doubt that cesarean section is now a much safer operation than formerly, both for mother and baby, not only for the reasons mentioned by the author, but because of better diagnostic skill, so that fewer patients are brought to surgery in a neglected condition.

We no longer take pride in performing a difficult midforceps operation and coming forth with a live baby that looks like a well-used or abused manikin. Certainly, abdominal delivery is much easier on the patient and operator, and the use of cesarean section should be increased if too many midforceps operations are being done.

At West Suburban Hospital the fetal and maternal mortality rates are lower with elective cesarean section than with vaginal delivery. This feeling of security should be carefully studied, however, as many other reports do not agree. At Bellevue Hospital, the corrected infant mortality in cesarean section was twice that of vaginal delivery.

At the Chicago Lying-in Hospital, neonatal mortality for cesarean section is three times the average rate at that institution. Resorption atelectasis accounted for all but three of the infant deaths. Pulmonary complications seem to be the great hazard with elective section.

There seems to be some mechanism in vaginal delivery which conditions the pulmonary system for normal function. With a cesarean section this often is lacking, and it predisposes the pulmonary tree to a condition similar to that in the premature infant.

In a recent report from Houston, babies having been through a trial of labor showed much less respiratory difficulty than those delivered by elective section. Certainly, a well-conducted trial of labor is warranted on all patients with a borderline disproportion.

Another hazard in elective section is that of proper timing. The date of operation is often set before term and many times the baby may be more premature than was expected.

A further risk in future pregnancies is that of a uterine scar rupturing before termination of the pregnancy, with the loss of the baby and great danger to the mother.

At Evanston Hospital from 1930 to 1950, in a group of almost entirely private patients, the average rate for cesarean section was 4.14 per cent and is no higher now than in 1930.

The corrected maternal mortality rate was 0.45 per cent. The major indications were as follows: repeat section 37.3 per cent, disproportion 22.5 per cent, toxemia of pregnancy 11 per cent, placenta previa 8.3 per cent, and premature separation of the placenta 3.9 per cent.

Our uncorrected fetal mortality for vaginal delivery was 3.0 per cent, and 7.3 per cent for cesarean section. The uncorrected fetal death rate for midforceps operations from 1940 to 1950 was 2.4 per cent, from which I conclude we are not delivering many women by midforceps who should have abdominal delivery. Ninety-seven per cent of our sections were the low cervical type. In this series general anesthetic was used in 82.5 per cent, spinal in 11.9 per cent, and local in 5.6 per cent. We now use spinal, however, in 70 per cent of our vaginal deliveries and in most of the cesarean sections.

I would consider the following suggestions as a means of perhaps reducing fetal mortality with cesarean section: (1) the use of regional anesthesia wherever possible; (2) careful selection of the proper time for elective section to avoid prematurity; (3) allowing a trial of labor when feasible; (4) postural drainage and suction of the baby's airways, plus liberal use of oxygen, and aspiration of stomach contents when indicated.

DR. WILLIAM J. DIECKMANN.—Elective cesarean section is supposed to result in a live and healthy mother and baby. Dr. Carey's results are no better than ours and I am not pleased with our neonatal mortality after cesarean section. I am not certain about all of his data but as well as I could determine 96 of the deaths in vaginal deliveries after 36 weeks were presumably preventable. In 31 the pathologist could not find any reason for death. Nine or more of the deaths of 69 babies born by cesarean section after 36 weeks were presumably preventable. These neonatal deaths were in near-term babies with presumably no pathologic cause for death and are the cases in which the obstetrician in some way is the cause.

Many of these babies born by cesarean section at autopsy are found to have a hyaline-like membrane in the lungs and death is ascribed to pulmonary pathology. I have thought for many years that this is a terminal phenomenon and that there is an initiating cause which may be cerebral. I recall that in the first cases we thought the babies had an intracranial injury since the symptoms and signs were typical. We have given the babies born by cesarean section all the blood out of the placenta and in addition have transfused them immediately after birth. Another group were given concentrated serum albumin when the first evidence of pulmonary pathology appeared. Nothing helped —the babies died in six to twenty-four hours after operation.

During the past year we have performed the cesarean section nearer to term than our previous 38 weeks' time and have in addition dehydrated the mother. In normal labor there is a weight loss of 500 to 1,500 grams. We have dehydrated by limiting fluid intake to 1,000 ml. for the 24 hours preceding the operation; have had the patients on 8 Gm. of ammonium chloride per day for the preceding 4 days or have limitation of fluids and a diuretic in the preceding 24 hours. In 24 hours, patients have lost from 35 to 3,225 grams. All of the babies survived but the series is small (25). (Patients were skin tested for sensitivity to mercury.)

DR. JAMES E. FITZGERALD.—Why did you do a repeat section at 28 weeks? Were you worried about rupture of the uterus?

DR. HENRY BUXBAUM.—What do you mean by cephalopelvic disproportion when the baby weighed only 3 pounds, as mentioned in your fetal mortality?

DR. CAREY (Closing).—In answer to Dr. Buxbaum's question, this patient had a true rachitic pelvis, with a posterior sagittal measurement of 8; hence it would have been impossible to have delivered her from below.

Dr. Fitzgerald asked why we did a repeat section at 28 weeks. I examined this patient and she was in active labor. Following our policy of repeat section, and considering the possibility of rupture of the uterus, she was operated upon.

We, too, are unhappy about our mortality in full-term infants. In our last obstetrical conference we discussed this in detail. What are we going to do today? We are losing too many full-term babies.

THE ROLE OF DÜHRSSEN'S INCISIONS IN PROLONGED LABOR*

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OVER the years, the use of Dührssen's incisions has been commended under certain circumstances. Of those papers presented before specialty societies and submitted to discussion, however, one finds the voice of some of the discussants raised to decry the operation and condemn its use. The publications by Hunt and McGee in 1936, Douglass and Graves in 1948, and Evans and Stander in 1954 stand out in presenting the value of the procedure. This study was prepared to evaluate the procedure and determine its range of usefulness on the services of the Chicago Maternity Center.

The Chicago Maternity Center delivers annually approximately 3,000 women in the home. The medical personnel at the Center respond to any and all obstetric calls within the limits of the City of Chicago. A significant number of patients are unregistered and some calls are received from private physicians and midwives. The patient group served are the underprivileged where minimal health levels are present. Few medical services exist that present as many knotty and bizarre problems. In cases requiring operative delivery, all modern and essential equipment, blood, instruments, oxygen, anesthetic agents, and plasma are transported to the patient's home. A competent obstetrician, a resident, an obstetrical nurse, and students are present on all problems of dystocia. During the past 20 years, there have been 55,557 home deliveries. The cases of Dührssen's operation were analyzed on an overall basis as well as in so-called early and late periods. The earlier cases are grouped into a fifteen-year period (1932 to 1947) and compared to those of the last five years (1947 to 1952), to see the major trends regarding this procedure that have been established during the interval.

Data and Results

In this study (Table I), every case in which a surgical incision was made into the cervix in labor to facilitate delivery has been reviewed. Those cases in which Dührssen's operation was used exclusively for fetal indication were excluded from the discussion. The data indicate that the Dührssen's operation was utilized principally in the primigravid young woman in labor at term. Labor was initiated spontaneously and the factors which ultimately necessitated operative interference were seldom determined or successfully evaluated during the prenatal period. The babies delivered were of average weight and this factor played no important role in the ultimate outcome. The incidence of the operation was low in the early period and during the past five years there was a further decrease with a corresponding increase in the incidence of cesarean section.

*Presented at a meeting of the Chicago Gynecological Society, Feb. 19, 1954.

TABLE I

	JULY, 1932-JUNE, 1947		JULY, 1947-DECEMBER, 1952		20 YEAR PERIOD	
	NO.	%	NO.	%	NO.	%
Total deliveries	36,655		18,922		55,577	
Cervical incisions	110	0.30	39	0.21	149	0.27
Total cesarean sections	328	0.89	283	1.50	611	1.10
Age (Years).—						
Average	24.1		24.8		24.3	
Youngest	14		14		14	
Oldest	38		44		44	
Parity.—						
0	85	77	31	79	116	78
i	7		2		9	
ii	7		1		8	
iii and over	11	10	5	13	16	11
Prognosis.—						
Normal spontaneous delivery	79		25		104	
Guarded	16		4		20	13
None recorded	15		10		25	16.7
Duration of Pregnancy.—						
Premature	3		2		5	
Term	107		37		144	
Post-term	0		0		0	
Onset of Labor.—						
Spontaneous	106		39		145	
Induced	4		0		4	
Weight of Babies.—						
Up to 6½ pounds	20	(2 sets of twins)	9		29	19
6½ pounds—8 pounds	61		20		81	54
Over 8 pounds	31		10		41	27

TABLE II

	JULY, 1932-JUNE, 1947		JULY, 1947-DECEMBER, 1952		20 YEAR PERIOD	
	NO.	%	NO.	%	NO.	%
Cervical Incisions.—						
Location 10-2-6	81	73.6	29	74.3	110	73.8
10-2	19		4		23	
Others	10		6		16	
Extension of incisions			4			
Healing of Cervix.—						
Well healed	53		28		81	54.4
Unsatisfactory	18		3		21	14.1
No follow-up	39		7		46	30.8
Unrepaired	0		1		1	
Method of Repair.—						
Interrupted	110		14		124	
Continuous	0		24	61.5	24	
Unrepaired	0		1		1	
Excessive Blood Loss.— (Third stage, over 500 c.c. estimated)	13	11.8	4	10.3	17	11.4
Transfusions given	3	2.7	1	2.6	4	2.7

The method (Table II) used in performing Dührssen's incisions varied but little from those described in the literature and the standard textbooks of obstetrics. Generally, the cervix was cut at three sites, 2, 6, and 10 o'clock between 8 inch clamps or ring forceps under direct vision, and the incisions were carried to the vaginal fornices. When possible, the 6 o'clock incision was made first, and after the three incisions were completed the diameter of the cervical ostium was equivalent to complete dilatation. It will be noted that during the past five years, if the cervix was not incised to the fornix or fewer than three incisions were made, extension of the incisions occurred in four out of ten such cases. If three incisions were made and carried to the fornices, extension did not occur. Bleeding was found to be practically nil in the completely effaced cervix. The repair in the earlier group was done with interrupted catgut sutures; however, during the past five years the majority of the repairs have been done with the use of continuous catgut sutures, either locked or unlocked. In general, the latter group healed much more satisfactorily, but this could be associated with the recent advent of effective antibiotics and earlier termination of labor rather than the method of repair. When the "clover leaf" deformity did occur in a poorly healed cervix, this could, in most cases, be adequately corrected with cauterization. The blood loss in the third stage of labor is increased in this group of patients; there was no appreciable increase, however, in the bleeding from the episiotomies that accompanied this procedure and bleeding of consequence from the cervical incisions was rarely encountered. The increase in blood loss is, therefore, ascribable to intrauterine hemorrhage and appears to be a concomitant of prolonged labor and uterine inertia. Transfusions were rarely needed but, during the past five years, blood has always been immediately available, when this procedure was contemplated in our prolonged-labor group.

TABLE III

ANESTHESIA	JULY 1932-JUNE 1947		JULY 1947-DECEMBER 1952		20 YEAR PERIOD
	NO.	%	NO.	%	
Parasacral	87	79.1	10	25.6	97
Saddle block	0		23	58.9	23
Ether	10		3		13
Parasacral and ether	4		1		5
Pudendal block	2		1		3
Pudendal block and ether	3		0		3
Saddle block and ether	0		1		1
None	4		0		4

As indicated in Table III, the majority of these operations during the first fifteen-year period were accomplished under parasacral block anesthesia. During the past five years, there has been a marked change. A majority of the cases are now done under saddle block anesthesia. A regional anesthetic is especially desirable on a service such as at the Chicago Maternity Center. These anesthetics afford pain relief plus adequate relaxation of the pelvic musculature, and at the same time the patient's welfare is safeguarded from prolonged inhalation anesthesia. Saddle block anesthesia has proved effective for the performance of the Dührssen's operation, even when associated with rotation and midforceps delivery, although some of the men at the Center still prefer parasacral block anesthesia.

Within the past five years, we have found that 72 per cent of patients went into labor spontaneously with the head unengaged (Table IV). Since this group is made up of a preponderance of primigravid women (79 per cent), this is an unusually high incidence. The usual incidence given for this group

is 6 to 10 per cent.[4] Coupled with this we find that at the time of the beginning of the operative procedure, of those babies in cephalic presentation, 83 per cent were in either the posterior or transverse position. This incidence was practically the same when the first fifteen years are compared with the past five years. Of the remaining 17 per cent, it is impossible to estimate what proportion of these started as posterior or transverse and finally ended up as anterior after a prolonged labor.

TABLE IV

POSITION AND PRESENTATION AT ONSET OF OPERATIVE PROCEDURE	JULY, 1932-JUNE, 1947		JULY, 1947-DECEMBER, 1952		20 YEAR PERIOD	
ODP	39		18		57	
OLP	36	84 cases	4	28 cases	40	112 cases
ODT	6	(85%)	1	(78%)	7	(83%)
OLT	3		5		8	
ODA	4		3		7	
OLA	11		5		16	
Transverse (version and extraction)	5		1		6	
Breech	4		2		6	
Not recorded	2		0		2	
STATION OF HEAD AT ONSET OF LABOR			1947-1952			
Unengaged			28 (72%)			
Engaged			11			

The average duration of labor in which Dührssen's incisions were used was forty-five hours (Table V); this was practically the same for the early and late periods. In a critical review of these cases, it was found that in many instances labor could have been terminated at an earlier period with less trauma to mother and child. During the past five years, it was noted that there was an average absence of progress of sixteen hours before labor was terminated. This is too long, if a higher fetal salvage is expected.

TABLE V

	JULY 1932-JUNE 1947	JULY 1947-DECEMBER 1952	20 YEAR PERIOD
Duration of Labor (Hours).—			
Average	45.0	46	45
Shortest	22.0	14	14
Longest	120	110	110
Absence of Progress (Hours).—			
Average		16 (8-30)	

Fetal Mortality

During the first fifteen-year period, 18 deaths occurred in 110 cases, or an incidence of 16.3 per cent. In the past five years there were five deaths in 39 cases or 12.8 per cent. The gross fetal mortality at the Chicago Maternity Center for the past twenty years was 2.98 per cent in fetuses of 1,500 grams and over. The gross fetal mortality associated with the Dührssen's operation appears at a glance to be very high; however, it seems both pointless and uninformative to present these percentage-wise and offer a corrected mortality. The Dührssen's operation was utilized in less than 0.3 per cent of the cases and one must concede that these were among our most formidable obstetric problems. In analyzing the fetal mortality, one is confronted with a complex problem of first trying to categorize those cases which were done for fetal in-

dication, and distinguish these from those done for maternal reasons, or a combination of both. Of the 23 dead babies, there were 5 dead at the time the procedure was started. The procedure was undertaken in these instances to terminate an extraordinarily long, ineffectual labor and was usually associated with a craniotomy. Of the 18 cases that remained, in only 8 cases was the infant considered in good condition at the start of the operative procedure. In these 8 instances, it is probable that the procedure contributed directly to the death of the infant. In the remaining 10 cases, there were 3 instances of pure fetal indication, and 7 instances where there was a combination of maternal and serious fetal distress. This latter group of 7 can be classified as "Dührssen's in extremis" and in this group the fetal mortality rate is prohibitive. It is in this type of case that refinement of diagnosis and evaluation are essential. Earlier termination by Dührssen's operation or earlier selection of cesarean section as a delivery method would yield better results. If an obstetrician is summoned in an extreme situation as described, Dührssen's operation may afford a useful method of resolving the obstetric problem.

Maternal Mortality

There was one maternal death in our series. The death, although it occurred shortly after the completion of the Dührssen's operation, was in no way caused by it. An autopsy revealed that death was associated with the deep ether anesthesia employed. In this particular instance, the delivery was very easy and there was no excessive bleeding from the cervical incisions, the episiotomy, or the uterus. A thorough examination showed no vaginal tears, no extension of the incisions, and no damage to the uterus.

Comment

The obstetric services at the Chicago Maternity Center are carried out on a very conservative level. The incidence of cesarean section during the twenty-year period studied was 1.1 per cent, and that of Dührssen's incisions 0.27 per cent. In the past five years, the incidence of Dührssen's incisions has decreased with a corresponding increase in the cesarean section rate. This has been a trend over the years in most institutions because of the progressive liberalization and greater safety of cesarean section as well as the use of intravenous Pituitrin. Dührssen's operation should be reserved for a small, well-defined group of cases. It should not, however, be considered an operation of despair, but rather another means of safely delivering a child. Deterioration of the situation is not a prerequisite for its use.

In analyzing our results, we find that a high percentage of our group can be classified as what we choose to call "typical cases." These cases are characterized as follows: The patient is a primigravida, with prematurely ruptured membranes, in whom labor ensues with an unengaged head in the posterior or transverse position. Labor is dilatory or tedious, actual labor alternating with periods of inertia, and, during the course of labor, in spite of supportive measures such as Demerol or morphine and intravenous fluids, labor becomes prolonged and progress fails.

The problem that confronts one is complex. We are dealing with a group of cases which may be classified as either the "persistent posteriors" or the "deep transverse arrests," which fall into the category of prolonged labor

with uterine inertia, and in which, in spite of the usual forms of sedation and intravenous fluids, labor fails to progress. Eliminating those in which there is cephalopelvic disproportion and cesarean section is indicated, we are still faced with a group of cases that need expert care.

Whether one considers twenty-four hours of labor as the dividing line of normal and prolonged labor, or eighteen hours as some have recently advocated, at this time a critical evaluation of the case should be carried out. As long as there is progress, labor is allowed to continue. If, however, progress ceases, the patient is given adequate sedation and intravenous fluids. If the membranes are still intact, they are ruptured artificially if the head is engaged, and the cervix 3 or more centimeters dilated.

In those instances of prolonged labor where there is a complete absence of progress for six to eight hours, a final evaluation should be made. If the head is not engaged and cannot be impressed well below the spines in a primigravid woman, a cesarean section is the method of choice. If the head is at plus 1 to plus 2 station and there is no cephalopelvic disproportion, there are still several choices: (1) further labor, (2) intravenous Pituitrin, and (3) Dührssen's incisions.

1. Further labor, with control of fluid balance, with or without additional sedation, will on occasion result in an easy delivery, but in a high percentage of cases undue procrastination will result in maternal fatigue and fetal embarrassment with a resulting high fetal mortality rate, irrespective of the method of delivery. We feel that the type of case under discussion should be terminated at the first indication of maternal or fetal compromise.

2. As to intravenous Pituitrin, insufficient experience has been acquired in cases such as are here described, so that this discussion must in part be speculative. If one is dealing, however, with a situation in which the conditions warrant the termination of labor by Dührssen's operation, evidence of maternal exhaustion or fetal embarrassment would make the use of intravenous Pituitrin an unwise choice. These patients should be delivered expeditiously to prevent further deterioration of the situation. Furthermore, the accentuation of uterine contractions in the presence of a persistent positional dystocia may seriously compromise the fetus. If the potential problem we are confronted with can be evaluated early, however, intravenous Pituitrin might prove very useful in a number of these cases, if used soon after failure of progress. Only further observations on the type of case under discussion will provide the answer.

3. Dührssen's incisions, during the past five years, have been undertaken sooner when the conditions are present that would permit the termination of labor. This we feel is a desirable trend since our experiences indicate that continuing failure of progress results in maternal fatigue and fetal embarrassment with a consequent high fetal loss. We find, therefore, that, given a situation in which the conditions for Dührssen's incisions are present, the operation is not difficult and offers a successful method for the termination of labor. After the patient has become completely exhausted and evidence of

fetal distress has occurred, the Dührssen's operation was followed in some instances by the death of the infant, not because of the trauma of the procedure, but because of the damage which the fetus had already incurred.

In analyzing the fetal mortality we find that some cases were poorly chosen, and in others the operation was used to terminate an extreme situation. However, in those cases in which the conditions were such as we now consider essential, there was practically no fetal loss associated with the procedure. In only one instance were the indications we now advocate satisfied.

In passing it may be appropriate to mention here the effectiveness of this procedure for fetal indications if the conditions necessary for vaginal delivery are present.

Summary and Conclusions

This study of a twenty-year period demonstrates that there are certain factors predisposing to prolonged labors which may require Dührssen's operation, and we attempt to set forth the conditions necessary for its successful use. The factors that have been most consistently involved in the causation of the prolonged labors are: (1) premature rupture of the bag of waters; (2) the onset of labor with an unengaged head in the primigravid woman; (3) the occipitoposterior or transverse position; (4) a desultory type of labor with inertia; (5) a cephalopelvic ratio of 1:1 with positional dystocia.

A plea is made for earlier interference to assure a higher fetal salvage. It was surprising to find that saddle block anesthesia is adequate for this procedure, which should consist of three incisions to the fornices. Bleeding from the effaced cervix was never a problem, and healing was surprisingly good, especially during the past five years. Better healing was associated with the routine use of effective antibiotics, earlier definitive action, and the use of a continuous suture.

Over the years, the criteria used for the termination of cases by Dührssen's incisions have varied. Many of the cases were poorly chosen and this accounts in part for the high fetal mortality. Another factor, of course, was the use of this procedure ten to twenty years ago to avoid cesarean section in mishandled cases. After a careful review of our results, we feel that if the following criteria are present, there would be no increase in fetal mortality nor damage to the mother: (1) no cephalopelvic disproportion; (2) complete cervical effacement; (3) fetal skull at plus 1 to plus 2 station; (4) dilatation of 5 cm. or more; (5) absence of progress with ruptured membranes for at least six to eight hours after adequate sedation and maintenance of fluid balance.

We feel that incising the cervix, correcting the malposition, flexing and rotating the head, and then doing a gentle forceps delivery will cause no fetal damage, and that appropriate repair of the maternal parts leaves the patient uninjured for further normal childbearing.

Cesarean section and intravenous Pituitrin should not compete with the use of the Dührssen's operation in appropriately selected cases. The operation should not be considered a procedure of desperation, and fetal embarrassment and maternal exhaustion are not prerequisites for its use.

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Discussion

DR. WILLIAM F. GEITTMANN.—The authors are to be commended for refreshing our thoughts about Dührssen's incisions. This is one of the obstetrical procedures which has been condemned by such statements as we have heard from this podium that "it is an admission of a mistaken diagnosis." I am sure that we will all agree that this is true as evidenced by the fact that approximately 75 per cent of these patients who had Dührssen's incisions had a prognosis for a normal spontaneous delivery. Last year we presented a paper before this society on our experience with the treatment of placenta previa at Cook County Hospital. In it we pointed out that there were other methods of treating placenta previa, such as the Voorhees bag, Willett forceps, rupture of the membranes, and Braxton Hicks version, and not only "transfuse and section." Likewise, I feel there is still a place for the procedure of Dührssen's incisions in our obstetrical armamentarium. In a service such as that conducted at Cook County Hospital and the Chicago Maternity Center the use of Dührssen's incisions can be a lifesaving measure. I am sure that occasions arise in all of our practices in which rapid delivery is necessary and Dührssen's incisions can be employed successfully on an incompletely dilated cervix.

There were four patients in the earlier series in whom labor was induced and I presume it was for good medical reasons. In the literature many of the Dührssen's incisions were made after induction. I feel that induction should not be done in primiparas unless the cervix is very ripe and the physician has a good medical or obstetrical reason.

In this paper the statement is made that "the babies in this series were of average weight and played no important part in the ultimate outcome." I do not agree with this statement as it is not true. We do not have a true evaluation of these pelves and a 5½ pound baby could be too large for some pelves. It was my impression in looking over our cases of Dührssen's incisions at St. Luke's that most of the trouble was with large babies and a midpelvis contraction or a funnel type of pelvis. The usual story was a large baby, head seemingly entering the pelvis well, poor labor, an effaced cervix which slowly dilated to 6 to 7 cm. and then stopped dilating. In these instances my feeling was that the cervix could not retract over the head to complete dilatation because the cervix was jammed against the sides of the pelvis by a too large head. These patients all had Dührssen's incisions, a hard forceps rotation, postpartum bleeding, and a stormy course for mother and baby.

Any primipara at term who enters labor with an unengaged head bears sharp watching as the head should be engaged at that time. True, many of these heads will descend and be delivered without difficulty but one must be alert in these cases.

In the last five years the fetal mortality in patients who had Dührssen's incisions was 12.8 per cent. Seventy-two per cent of these patients had unengaged heads on going into labor and 80 per cent of them were primiparas. I feel these cases were the result of poor or negligent obstetrics.

I would also like to ask the authors about the oldest patient in the last five-year series. Was she a primipara? How long was her labor?

In considering the fetal mortality, I feel that the procedure was justified in the 10 cases of Dührssen's in extremis because no other procedure was safe at that stage. The 8 whose infants were in good condition, however, should have had cesarean section. These were probably cases of disproportion or the delivery might not have ended fatally for the babies.

The maternal death the authors state was in no way connected with the procedure of Dührssen's incisions but it is the same old story. If the patient hadn't needed Dührssen's she wouldn't have needed the deep ether anesthesia which was the cause of death.

I would like to ask the authors why the patients with transverse presentations had Dührssen's incisions, and were the babies dead or alive?

In closing, I agree with the authors that when we can make an early diagnosis of prolonged labor we should do more cesarean sections. I feel too that Pituitrin by intravenous drip should be used earlier in inertia of labor and was not advisable at the time these Dührssen's incisions were done. The conditions must be rigidly adhered to for the successful use of Dührssen's incisions. I would like to make one suggestion which has proved helpful in the delivery of patients when the cervix is dilated 7 to 9 cm., persists there for several hours, and becomes edematous. The cervix can be gently pushed up over the head with the pains and a rapid delivery will follow. I know some of you will say "manual laceration"; but it can be done gently and effectively without lacerations.

DR. HARRY BENARON.—I would like to remind the authors that Alfred Dührssen was also famous for other things than incision of the cervix. He introduced the operation of vaginal cesarean section, and in addition popularized the performance of episiotomy in vaginal delivery.

The incidence of incisions of the cervix herein reported was 2.7 per cent over a twenty-year period, while for the same period the rate of cesarean section was 1.1 per cent. I think it is important to correlate the incidence of both procedures since they are definitive in the treatment of prolonged labor.

The indictment of incision of the cervix as a procedure by the discussant, Dr. Geittmann, on the basis of too high a fetal mortality, is, in my opinion, misdirected. Evans and Stander in 84 cases quoted an incidence of 6.6 per cent—over three times the rate quoted by the authors, and their fetal salvage was a remarkable 95.35 per cent. It seems obvious to all, therefore, that an improvement in the fetal mortality rate would be achieved by increasing the incidence of the operation, rather than by condemning it; by terminating earlier rather than later—by whatever method is expedient.

It was brought out that prenatal care did not in any way help the management of these cases. That is as one would expect. It is impossible to foretell the mechanism of labor. The production of complete dilatation of the cervix is accomplished by the powers of labor, modifying factors being the anatomy of the cervix, the pelvic architecture, and the presenting part.

Certain technical aspects must be stressed. The amount of dilation present is of no moment at all. Some proponents of the procedure, including the authors, demand a certain minimum degree of dilation. There is no valid reason put forth for such a view. The only requirements to my mind—and this is the "sine qua non" of the procedure—is that there is present complete effacement of the cervix and engagement of the head. If done under these circumstances the cervix will not bleed. Also to save blood loss it is wise to delay the performance of episiotomy until after the cervix has been incised. Do not forget to evaluate the case thoroughly before proceeding—rule out constriction ring as a cause of prolonged labor—incising the cervix will not help. Use a regional anesthesia method—it permits of a deliberate, careful technique, and is better for the baby.

In presenting this method of terminating prolonged labor I would like to see the authors correlate the length of labor with the fetal loss. At what point in time is there a sharp rise in fetal mortality? This I believe is the crux of the situation.

To my mind the presented data suggest that incisions of the cervix as a step in the termination of prolonged labor are safe for the mother. A better fetal salvage than presented by the authors would be forthcoming if earlier interference were practiced.

DR. RALPH A. REIS.—This interesting and apparently perplexing subject makes me wonder, as I hear the title and listen to the paper, whether the time has not come to give consideration to a change in nomenclature. There are few of us who can pronounce the name "Dührssen." There are fewer of us who understand exactly what Dührssen recommended in 1890. There is practically no one who can spell his name in English. Therefore, it seems to me that we should change the name to cervical incision. I think it would be more descriptive and would serve our purpose better.

DR. ROBERT M. GRIER.—I feel rather strongly on the abuse of Dührssen's incisions. The frequency of their use in this report shows that the authors have been conservative.

I am inclined to be sympathetic, however, with the people who are handling deliveries in the home. All too often "so-called" conservative management of a woman in labor is carried to the extreme. Both fetal and maternal distress may appear when only an obstinate cervix is the cause. In some of these women Dührssen's incisions can be a life-saving procedure. I do not think incising the cervix under these conditions is any worse than manual dilatation from 7 or 8 cm. dilatation to completion, which very often results in lacerations. Let us not be too critical of these poor fellows in the district service. It would often be too late if the patients were sent to a hospital with all the delay so often involved.

DR. M. EDWARD DAVIS.—It is very nice of Dr. Grier to be charitable and feel sorry for the people who deliver babies in the home. The use of Dührssen's incisions need not be confined to home deliveries, however, for the operation still has a place in good operative obstetrics. I know that there are institutions in which this procedure has never been done and traumatic manual dilatation of the cervix or cesarean section replaces it. Abnormal delivery should not be used as a way out of every obstetrical complication, however.

There are patients who have no cephalopelvic disproportion but who have faulty labor mechanisms. Cervical dilatation progresses to a certain point beyond which no further progress occurs. The head is deeply engaged in the pelvis, often resting on the perineum and in a posterior position. Additional hours of labor result in no further cervical dilation but the cervix develops increasing edema which actually decreases the amount of dilatation. Manual dilatation of such a cervix is traumatic and nineteenth-century obstetrics. Attempting to pull the head forcibly through such a cervix will not only result in serious tears but will wreck the normal supports of the uterus and environmental viscera. What is more logical and in line with modern thinking than to make two or three surgical incisions in the cervix and deliver the baby easily and safely? Why well-trained, highly competent obstetricians who do the most extensive radical surgery balk at such a simple procedure I cannot explain.

Dührssen's incisions are repaired easily and usually heal nicely. Poor healing does not interfere with the normal function of the cervix. Subsequent labors and deliveries are most likely to be easy and uneventful.

Cesarean section should be the procedure of choice when there is any evidence of cephalopelvic disproportion, when the presenting part is in the midpelvis, and when there are other factors which would result in a difficult delivery.

DR. WILLIAM G. CUMMINGS.—One point that impressed me during the whole discussion was this: It seems to me that there is no real connection between Dührssen's incisions and cesarean section. I do not see why cesarean section is ever indicated in place of Dührssen's incisions. If there is disproportion what good are Dührssen's incisions, followed by a traumatic forceps delivery? I have never used this operation because I do not like to see a scarred cervix. If the cervix can dilate to 8 cm. I can slip it over the head without a tear.

THE CASE FOR MIDFORCEPS*

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(From the Evangelical Deaconess Hospital)

IN THE past few years, the increasing safety of cesarean section has necessitated a new evaluation of its indications. Articles have appeared from many clinics reviewing their results. D'Esopo,[1] in one of the best, reviewed the experiences at the Sloane Hospital. He was able to report 1,266 cesarean sections with only one maternal death, and this in no way attributable to the operation. With such a degree of safety in cesarean section, he felt that more consideration could be given to the infant in the indications, in deliveries which might be unduly traumatizing to the baby even though not necessarily fatal. He stated that, in his clinic, version and breech extraction and high forceps operations are now considered obsolete and he felt that midforceps might soon join them. He showed graphically that in the past few years, as the incidence of cesarean section had gone up and that of midforceps had gone down, the percentage of preventable fetal mortality and morbidity had fallen. D'Esopo felt that, in his clinic, in order to keep the incidence of preventable fetal deaths under 1 per cent, it would be best to keep the incidence of cesarean sections at about 6 per cent and of midforceps operations under 1 per cent. He suggested that each group should review their results and arrive at an average individually best for them.

Taylor[2] reviewed the results of 31 midforceps operations performed during 10,055 consecutive deliveries at the Colorado General Hospital and the Denver General Hospital from Jan. 1, 1948, to May 1, 1953. Eight infants were stillborn or died from birth injury soon after delivery, a mortality rate of 26 per cent. Seven others received major birth trauma but lived. There was also a high incidence of trauma to the mothers. Considering these results, he felt that midforceps operations should probably be entirely eliminated. He advocated the use of intravenous Pituitrin drip as being safer than the forceps operation and felt that those cases in which the presenting part could not be brought to a lower station in that way should be treated by cesarean.

On the other hand, several authors have presented impressive series of midforceps operations with creditable results. Weinberg[3] reported 1,150 midforceps deliveries with a fetal mortality of 0.7 per cent, a result better than in any series of cesarean sections with which he was familiar. These deliveries were performed at several hospitals and by various operators but the author was personally concerned in each delivery in some connection. He stressed the fact that all of these patients had x-ray measurements of the

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pelvis so that cases of actual disproportion were eliminated. In 40.8 per cent of his cases the operation was needed because of dystocia arising from a malpresentation, usually a transverse arrest or a persistent posterior. Dennen[4] reported 527 midforceps operations performed in a series of 11,777 viable babies delivered at the New York Polyclinic Medical School and Hospital, an incidence of 4.48 per cent. He had a corrected fetal mortality of 2.27 per cent and no maternal deaths. These cases were done by sixty-one different operators over a ten-year period.

Material

This review was undertaken in an attempt to crystallize our personal opinions in this rather changing and conflicting field of thought. We have analyzed the results obtained in 2,477 consecutive deliveries in the practice of the senior author from July 1, 1948, to July 1, 1953. All patients were followed throughout pregnancy and were delivered personally or by an alternate if he was out of town. The deliveries were performed at Evangelical Deaconess Hospital, Fairview Park Hospital, and St. John's Hospital, all in Cleveland. Cases seen in consultation were not included, because in them a different type of delivery is sometimes required than would have been elected had the case been seen earlier. While this series is small compared to those presented by certain clinics, it does offer the advantage of uniform selection of cases and uniformity of operative ability.

There is at present no unanimity of opinion as to what constitutes a midforceps delivery and it is necessary to define our terms. The midplane of the pelvis is accepted as being at the level of the ischial spines. Weinberg[3] has pointed out that from this level to the plane of the inlet is approximately 7.3 cm. and that from the lowest bony point of the well-flexed head to its biparietal or largest diameter averages 5 cm. Therefore, if the lowest bony point of the head is within 2 cm. of the spines its largest diameter has passed the inlet. He defines forceps deliveries as follows:

1. Mid—The most dependent bony portion of the flexed head is between the level of the ischial spines and the ischial tuberosities.
2. High—The presenting part lies between the inlet and the spines.
3. Low—The presenting part is below the tuberosities.
4. Floating—The presenting part is above the inlet.
5. Outlet—The presenting part is easily visible and distending the perineum and vulva.

We feel that this is one of the best definitions offered since bony landmarks are used to identify each station. The criteria we have followed are shown in Fig. 1. It can be seen that our definitions correspond closely to those of Weinberg except that what he terms high, we have called high mid. In other words, if the most dependent bony portion of the presenting part was 1 or 2 cm. above the spines, we felt that the head was engaged and termed the station high mid. Above this station, forceps operations were not used as the method of delivery.

In preparing our tables we have used approximately the definition of preventable fetal mortality suggested by D'Esopo.[1] He arrived at this figure by taking the over-all fetal mortality and excluding immature infants (under 1,000 grams), those dead in utero before the onset of labor, and those with congenital defects incompatible with life. We have extended this slightly

and, instead of excluding those dead before the onset of labor, have excluded only those showing signs of maceration. We felt this made the justification for exclusion a little more definitely demonstrable.

TABLE I. TOTAL MATERIAL STUDIED

		NO.	%
Total patients delivered		2,477	
Total number babies		2,503	
Spontaneous		53	2.11
Low forceps		2,138	85.01
Anterior	1,971		
Transverse	57		
Posterior (Modified Scanzoni)	110		
Midforceps		65	2.59
Twins		26	
With episiotomy		2,217	
Breech extraction		105	4.2
Version and extraction		43	1.72
On second twin	23		
Primary procedure	20		0.8
Cesarean sections		99	3.99

Table 1 gives a résumé of the entire material studied. By far the largest number of deliveries, 85 per cent, were by low or prophylactic forceps. There were 65, or 2.6 per cent, midforceps, while there were 99, or 4.0 per cent, cesarean sections. One hundred five babies, or 4.2 per cent, presented by the breech and were delivered as such, while in only 20, or 0.8 per cent, a version and breech extraction were done as a primary procedure. Of the midforceps deliveries, 7 were classified as high mid, 31 as mid, and 27 as low mid.

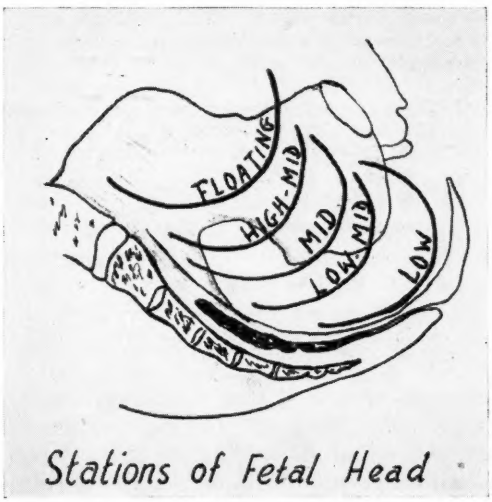

Fig. 1.

In Table II, some pertinent facts concerning the length of labor in the cases delivered by midforceps are presented. We have defined prolonged labor as that in which both the first and second stages took more than twenty-four hours. In our entire series, the number of labors thus prolonged was 3 per cent. In the 65 cases terminated by midforceps, there were 15 labors of more than twenty-four hours and 7 of more than forty hours, a total of 22 cases of prolonged labor, or almost one-third of the entire number. The maximum was fifty-three hours. Likewise, we have felt that a second stage of more than

two hours was prolonged. By this definition 28 of the 65 cases had a prolonged second stage and in 15 it was more than four hours, with a maximum of seven hours. Two never reached the second stage. One of these was delivered after manual dilatation and the other after Dührssen's incisions.

TABLE II. LENGTH OF LABOR, 65 CASES

I. Combined First and Second Stages.—		
24 hours and over		15
Over 40 hours		7
Total		22
Maximum	53 hours	
II. Second Stage.—		
2 hours and over		28
Over 4 hours		15
Total		43
Maximum	7 hours	

Indications

In selecting the indications for which our midforceps procedures were done we experienced considerable difficulty and may not have followed an entirely traditional pattern. There is certainly considerable overlapping between some of the groups, and in many cases more than one indication was operative. We have selected the one which seemed to us most important. Of the 65 midforceps operations, 9 were in multiparas and 56 in primiparas.

TABLE III. INDICATIONS IN MULTIPARAS, 9 CASES

Positional, posterior, normal pelvis	3
Prolonged second stage, large baby, normal pelvis	3
Prolonged second stage, normal position, and pelvis questionable	1
Cyst of vaginal wall	1
Prolonged second stage, increased lumbosacral angulation by x-ray, plus narrow midpelvis	1

The indications for interference in the 9 multiparas are presented in Table III. In 3, the operation was necessary because of a persistent posterior position in a normal pelvis. In 3 others, the second stage was prolonged because of an oversized baby, although the pelvis seemed normal in each case. In one, the second stage was somewhat prolonged although the baby was of normal size, in normal position, and the pelvis seemed normal. This case was classified as questionable, the meaning of which term will be explained later. In one, dystocia was caused by a soft cyst in the posterior vaginal wall. After delivery the cyst had disappeared and did not return. In one a difficult midforceps delivery was necessitated by a large baby in a pelvis shown by x-ray to be narrow in its mid-portion. This case will be referred to again later.

The primiparas are analyzed in Table IV. In 17, there was x-ray evidence of some pelvic contraction. This was almost always reported as a shortening of the interspinous diameter, in other words, a narrowing of the midpelvis. In 21, the pelvis was normal both clinically and by x-ray and the dystocia was considered due to malposition of the baby's head. In this group plus the former group of pelvic contractions, there was a total of 38 cases. There were 30 cases of malpresentation. In others words, in the primiparous patients, malpresentation of the fetal head was a factor in over half the cases. Prolonged labor, soft-tissue dystocia (not cervical) and large baby accounted for 4 cases each. We ended up with 6 cases which we grouped as miscellaneous. Two

patients were elderly primiparas who were allowed to have prolonged labors and come to midforceps operations because the fetus was in a normal position and the bony pelvis was adequate. One case was classified as uterine inertia. In one there was a clinically contracted pelvis but the labor was not prolonged. In the 2 classified as questionable, it seemed in retrospect that the operation was probably performed because the patient had been improperly considered as being ready for delivery, was under anesthesia, and there were no serious contraindications. It will be noted that fetal indications were not used. There were undoubtedly situations when we were concerned for the baby's welfare but in reviewing these cases we chose something else as the primary indication.

TABLE IV. INDICATIONS IN PRIMIPARAS, 56 CASES

I. Pelvic contraction—x-rays		17
Transverse arrest	4	
Persistent posterior	5	
Anterior position	8	
II. Positional—normal pelvis		21
Transverse arrest	6	
Persistent posterior	15	
III. Prolonged labor		4
Normal position and pelvis	2	
Normal position, clinically contracted pelvis	2	
IV. Soft-tissue dystocia		4
Normal position and pelvis	4	
V. Large baby		4
Normal position and pelvis	4	
VI. Miscellaneous		6
Elderly primipara (40 plus years) with normal position and pelvis	2	
Uterine inertia	1	
Clinically contracted pelvis, labor not prolonged	1	
Questionable	2	
Grand total		56

TABLE V. MORBIDITY AND MORTALITY

Fetal.—	
Morbidity:	
Cephalhematoma	2
Facial paralysis, transient, and chephalhematoma	1
Facial paralysis, transient	2
Congenital deformities	2
Achondroplasia	1
Mortality:	
Congenital deformities (Spina bifida and hydrocephalus)	2
Corrected mortality	0
Maternal.—	
Morbidity:	
Temperature over 38° C. for 2 days	2
Cervical tear	2
Vaginal hematoma	1
Fractured coccyx	1
Postpartum pyelitis (Recovered)	2
Manual removal of placenta	1
Postanesthetic atelectasis	1
Mortality	0

Results

Table V presents the infant and maternal mortality in the 65 cases delivered by midforceps. There were 2 cases of cephalhematoma, one of transient facial palsy and cephalhematoma, and 2 of transient facial palsy. There were no major birth injuries. Two of the babies died following delivery but both had major congenital defects incompatible with life, giving a corrected fetal mortality of 0 per cent. There was no maternal mortality.

The mortality in cesarean sections performed in this series is shown in Table VI. There were 55, or 2.2 per cent, primary cesareans and 44, or 1.8 per cent, secondary, making a total of 99, or 4 per cent. The indications are not completely analyzed here but it may be seen that among the primary 14 were done for bleeding and 6 for x-ray evidence of disproportion without trial of labor. There was one stillbirth at term caused by premature separation of the placenta. There were 2 premature stillbirths and 8 premature neonatal deaths, most of which were at least partially accounted for by the condition necessitating the operation. The over-all fetal death rate was 11 per cent, which is practically unchanged by excluding the one congenital deformity. One mother died from hemorrhage following a cesarean section for central placenta previa, which had an area of accreta.

TABLE VI. CESAREAN SECTIONS

Total mothers			2,477	
Cesarean sections			99	3.99%
Primary			55	2.22%
For bleeding		14		
For cephalopelvic disproportion without trial labor		6		
Secondary			44	1.77%
Mortality.—				
Maternal			1.	1.01%
Fetal deaths			11	11.11%
Stillbirths			3	
Term		1 (Premature separation)		
Premature		2 (Premature separation)		
Neonatal			8	
Term		0		
Premature		8		
Toxemia	1			
Premature separation	3			
Placenta previa	3			
Hydrocephalus	1			

TABLE VII. MORTALITY IN BREECH EXTRACTION

Primary breech extraction			105	
Fetal Mortality.—				
Stillbirths		3		
Term	1			
Premature	2 (Both macerated)			
Neonatal deaths		2		
Term	1			
Premature	1			
Over-all mortality		5		4.75%
Corrected		3		2.80%
Maternal Mortality		0		

In the 105 breech deliveries summarized in Table VII, there was one term stillborn infant and 2 premature stillborn infants, both macerated, and one

death in a term infant and one neonatal death in a premature. This gives an over-all fetal mortality for breech deliveries of 4.8 per cent, corrected to 2.8 per cent. There were no maternal deaths.

TABLE VIII. MORTALITY IN INTERNAL PODALIC VERSION AND BREECH EXTRACTION

Fetal Mortality.—			
Total versions and breech extractions		43	
Second of twins		23	
Primary procedure		20	
Stillborn	0		
Neonatal	3		
1. Birth injury			
2. Erythroblastosis			
3. Anencephalic			
Total fetal mortality in primary procedures			15%
Attributable to procedure			5%
Maternal Mortality		0	

In the twenty versions and breech extractions done as primary procedures shown in Table VIII, there were 3 neonatal deaths, an over-all fetal mortality of 15 per cent. One death was due to erythroblastosis and one to a congenital anomaly, leaving one death, or 5 per cent, attributable to the operative procedure. No mothers died.

TABLE IX. ANALYSIS OF FETAL MORTALITY

Total babies born			2,503	
Total deaths			59	2.35%
Stillbirths		26		
Term	12			
Premature	14			
Neonatal		33		
Term	9			
Premature	24			
Nonpreventable deaths			25	1.00%
Stillbirths		19		
Term	10			
Premature	9			
Neonatal		6		
Term	3			
Premature	3			
Preventable deaths			34	1.35%
Stillbirths		7		
Term	2			
Premature	5			
Neonatal		27		
Term	6			
Premature	21			

TABLE X. CORRECTED FETAL MORTALITY IN EACH TYPE OF DELIVERY

I. Spontaneous	9.4%
II. Low forceps	0.6%
III. Breech	2.8%
IV. Internal podalic version	5.0%
V. Midforceps	0.0%
VI. Cesarean	11.1%

Table IX summarizes the fetal mortality for the entire series. Our over-all fetal mortality was 2.35 per cent, corrected to 1.35 per cent. The fetal mortality for each type of delivery corrected in this same way is shown in Table X. Of the one stillbirth and 4 neonatal deaths in the group of spon-

taneous deliveries, giving a fetal mortality of 9.4 per cent, all were early premature babies. Of the 2,138 infants delivered by low forceps, there was a total fetal mortality of 21, or 0.98 per cent. Eight of these deaths were classified as nonpreventable, leaving 13, or 0.60 per cent, as the corrected fetal mortality.

Comment

In determining the length of labor we have had the usual difficulties as to the indefiniteness of its onset. We have tried to use the establishment of pains sufficiently hard to cause changes in the cervix, either progressive dilatation or effacement or both, as marking its onset. Since we set two hours as rather arbitrarily limiting the length of a normal second stage and then allowed 15, or almost one-fourth of our cases, to go over four hours, a word of explanation is in order. Almost all of these patients received analgesia during labor and they sometimes reached full dilatation shortly after the last dose of analgesic drug. As a consequence, there might be very few voluntary expulsive efforts until the analgesia had lightened. We felt that, to be effectual, at least two hours should be spent in the second stage with hard pains and voluntary expulsive efforts, preferably with the membranes ruptured.

As to the actual mechanics of midforceps delivery, we have used Tarnier axis traction forceps routinely except in the simplest cases where very little traction was necessary. We feel that this rather ancient device is the most efficient instrument we know of for bringing a head through a tight midpelvis and outlet. Mid-transverse arrests were rotated with the solid-blade Tucker-McLane instruments or manually and then the axis traction forceps applied. Posterior positions were, with one exception, handled by rotating to the anterior with Bill's modification of the Scanzoni maneuver, using Tucker-McLane forceps and then reapplying the Tarnier blades. The one exception was misdiagnosed and delivery as a posterior was inadvertently carried out without any attempt at rotation. Kielland forceps were tried in years gone by but were discarded before this series was started. We feel that Bill[5] so adequately and completely described the technique of rotation from the posterior position with the use of the Tucker-McLane forceps that little has been added to the subject since. His classic paper on the subject has been somewhat lost as it was published in a short-lived journal.

Our use of the term uterine inertia and the decision whether or not to use pituitary extract to accelerate labor should also be discussed. Most series of midforceps operations include a rather high percentage of diagnoses of uterine inertia among the indications. We used it but once and feel a little apologetic about that. We feel that uterine inertia is a symptom and not a diagnosis and like to presume that if a well-flexed head is engaging in good position in a normally shaped and adequate pelvis, labor pains will be good and labor will progress normally. Poor or desultory pains, we feel, usually indicate something mechanically abnormal about the situation. Either there is some degree of malpresentation or some abnormality in the pelvic architecture, either bony or soft tissue, which prevents the head from being sufficiently well applied to the cervix to stimulate the contractions. This is illustrated by the frequent

change in the character of the pains following rupture of the membranes. Therefore, in cases of desultory labor, we feel that a complete re-examination and revaluation, including x-ray studies and frequently a sterile vaginal examination, are indicated. This will frequently disclose the underlying cause. Pituitary extract to intensify uterine contractions in either the first or second stage of labor was not used in this series. Although its use has recently been revived, the reaction of the uterus in labor to subcutaneous injections of even small doses of pituitary extract was long ago shown by Greenhill[6] to be unpredictable and dangerous. Reid,[7] who reintroduced its use, has already warned against it in certain instances.[8] We[9] believe that the use of intravenous pituitary drip to accelerate labor carries all the dangers inherent in any other form of its administration and have seen results to support our conclusions. It has been axiomatic among those using drugs to stimulate labor pains, ever since Stearns[10] introduced ergot for that purpose in 1808, that the drug should not be used unless the only thing abnormal was the strength of the pains. If such a revaluation as we have suggested is performed on patients in desultory labor, more and more abnormalities will be discovered and stimulating drugs used less and less. We feel that it is safer to increase slightly our incidence of midforceps operations or cesarean sections than to use the stimulating drugs during labor.

From our analysis of this series of cases, we feel that midforceps deliveries of considerable difficulty can be performed with a high degree of safety for both the mother and child. Our fetal mortality in the cases of midforceps was just as good as, or better than, it was in the breech deliveries or versions and breech extractions. Therefore, if we were to eliminate midforceps operations to reduce fetal mortality, we would also have to eliminate breech extractions and versions and the practice of obstetrics would consist of normal deliveries and cesarean sections. Another point in favor of retaining midforceps operations rather than terminating all of these cases by cesarean is the well-known fact that most of these women who have a difficult first vaginal delivery have a much easier time with subsequent deliveries. Of the 56 primiparous patients in this series we have delivered 25 a second time. In 24 of these, the succeeding labor was uneventful and progressed to a simple low-forceps delivery. The twenty-fifth was quite interesting. She had contraction of the midpelvis and outlet by x-ray. In her first labor she was delivered of a 7 pound baby by low forceps. In her second labor we had to do a rather difficult midforceps operation to deliver an 8 pound, 15 ounce baby. In her third pregnancy, the infant weighed 9 pounds, 4 ounces, and we had to perform a cesarean after an adequate trial of labor. Certainly the management was simpler the second time around than having 25 repeat cesareans.

We do not feel the necessity of any sweeping change in our indications for either midforceps or cesarean sections. In the analysis of cesareans we called attention to the fact that 6 were performed because of an x-ray diagnosis of pelvic contraction without a trial of labor. All of these occurred in the first two years of the series. Now we feel that all of them could safely

have been given a trial of labor and that probably several of them would have ended up as forceps deliveries. On the other hand, if repeated in the future, some of the longer labors might be handled by cesarean. Therefore, we feel that what we have learned is to continue the individualization of each case rather than to change the handling of any specific class of cases. We do feel that pelvic x-ray measurements should be done before any but the simplest midforceps operations to rule out definite disproportion. We also feel that trial forceps as suggested by Douglas and Kaltreider[11] has a place, though it was not necessary to resort to cesarean section after trial forceps application in this particular series.

Conclusion

We have analyzed a series of 2,477 consecutive patients delivered in private practice in an attempt to learn whether, in the interest of infant mortality, we should decrease our incidence of midforceps deliveries by the more liberal use of cesarean section. Since our infant mortality rate in the sixty-five cases delivered by midforceps was as good as or better than in any other type of delivery, we feel justified in continuing to use the procedure.

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CONTINUOUS PERIDURAL ANESTHESIA FOR CESAREAN SECTION*

A Report of 121 Cases

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PERIDURAL anesthesia has many advantages for cesarean section. Our experience with it has continued to be so satisfactory that we now report 121 additional cases. The importance of anesthesia in cesarean section is obvious, yet the dangers have not been sufficiently recognized.

The General Problem of Anesthesia in Obstetrics

We have been slow to realize that anesthesia is one of the principal causes of maternal death, and for a good reason. No matter how precisely it is stated on the certificate of death that the actual cause was anesthesia, death is allocated statistically to the antecedent condition, or to the diagnosis for which the anesthesia was administered. It has never been otherwise.[1, 2]

Nor can the hazard of anesthesia be measured by reports from well-organized obstetric services. Only regional maternal mortality committees, reviewing case reports as well as certificates of death, can furnish reliable evidence. Even then it is difficult. Death on the delivery table may have been due to anesthesia, but this may not at once be apparent. If sudden death should be due to the toxic action of the agent itself, it is easier to be reasonably sure of it than when death occurs in the course of inhalation anesthesia. Aspiration is a fairly common occurrence, not always easy to recognize clinically, and unless autopsy is performed within an hour or two of death, alveolar pathology may not be distinguished from common postmortem changes.[3] Death may not be immediate, and anesthesia, in the absence of knowledge of aspiration, may not be thought of as the cause of pneumonic areas, even though their distribution may be typical of postanesthetic atelectasis. Aspiration does not always precede atelectasis, nor does it always cause death. Davis and Gready,[4] reporting 2 maternal deaths from anesthesia, neither due to aspiration, found some 45 instances of aspiration during inhalation anesthesia; 8 patients were seriously ill but all recovered.

Acken[5] reported 11 deaths in 1,245 casearean sections. Eight of these deaths, nearly 73 per cent, were due to anesthesia.

Thompson,[6] reviewing 75 cesarean section deaths which had occurred in Los Angeles hospitals, found that one-sixth were due to anesthesia.

*Presented at a meeting of the Brooklyn Gynecological Society, March 17, 1954.

Recently, in Bronx County, a significant increase in the number of maternal deaths due to anesthesia has been reported.[7]

Hartnett,[8] analyzing 25 maternal deaths which occurred in five of the better institutions in St. Louis during the past five years found that anesthesia was responsible for 11, or 40 per cent of them; 73 per cent of these deaths from anesthesia were hidden in the hospital files under diagnoses difficult to find.

Hellman and Hingson[9] state, "While anesthesia and analgesia technics have in recent years improved the quality of obstetric pain-relief tremendously, the dangers of serious complications have likewise risen."

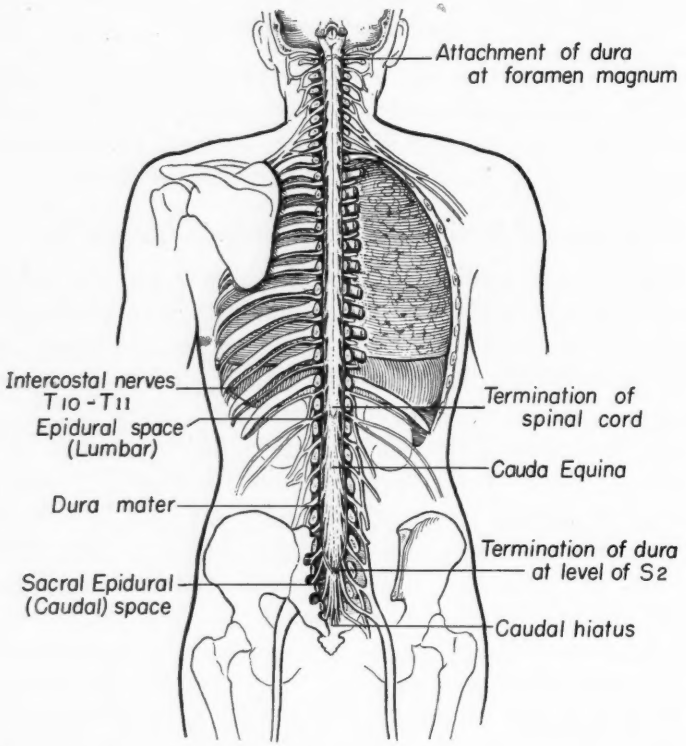

Fig. 1.—The peridural space extends from the foramen magnum at the base of the skull to the bottom of the sacrum. The spinal nerves traverse it on their way to their peripheral distribution. It varies from 3 to 6 mm. in size in different regions. (All figures from Ansbro and associates,[21] with permission of the *New York State Journal of Medicine.*)

In Brooklyn,[10] where for fifteen years puerperal mortality rates have paralleled the national trend, cesarean section has been concerned in approximately one-fifth of the deaths, and 20 per cent of the deaths during or after cesarean section were due to anesthesia. Atelectasis occurred almost as frequently with spinal anesthesia as with inhalation; there were no deaths from aspiration in the course of spinal anesthesia.

The risk of anesthesia is due not so much to the condition for which the operation is performed as to the skill and experience of the operator and the anesthesiologist. Steady increase in the number of cesarean sections makes

constant search for the best anesthetic more important. We have no perfect anesthetic but perhaps the quest is not a vain one. Eastman[11] thinks that anesthesia for cesarean section is one of the most important problems in obstetrics today. The greatest source of danger is the anesthetic.

In general, inhalation and intravenous anesthetics readily pass the placental barrier. Ether excites bronchial secretion and invites uterine atony. With cyclopropane the margin of safety is narrow, cardiac irregularities not uncommon, and the operating room should be explosion proof. Local block, the safest, is not suited to every obstetrician and its advocates find it unsatisfactory for the repeat operations which steadily grow in number. Spinal anesthesia, still dangerous in the hands of the thoughtless and the unknowing,

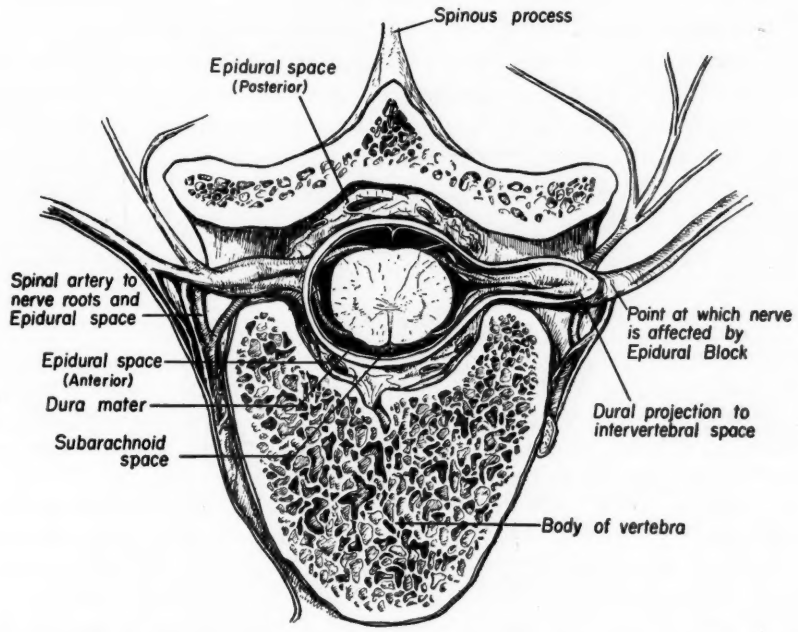

Fig. 2.—The peridural space. The envelope of dura covering the spinal nerves extends to the intervertebral space, at which point the anesthetic agent takes effect and blocks their afferent and efferent components.

has after many vicissitudes been rather widely accepted because of its advantages; yet it has been steadfastly rejected by Greenhill.[12] It is likely that reconsideration is again necessary, taking into account recent experience with saddle block.[13] Somewhat enigmatically it has been said[14] that "unless something is done, conduction anesthesia, in general, at least in the state of California, may have to be discarded."

Anesthesiologists who have made spinal anesthesia safer by use of oxygen, vasopressors, intravenous fluids, and control of the level of ascent have not been willing to discover and rely upon an anesthetic dose for cesarean section, small but calculated to be adequate for an operation performed for different reasons by all manner of operators. Continuous or fractional sub-

arachnoid block designed to meet this particular need should be safer, but is responsible for even more neurologic sequelae than single-dose spinal anesthesia and for more postspinal headaches.

General Advantages of Peridural Anesthesia

The dangers to which we call attention seem to us so particularly significant that the possibilities of the peridural space for anesthesia should be explored. The space is approximately 3 to 6 mm. deep and the dura, with proper technique, is relatively safe from inadvertent puncture (Fig. 1). The catheter is in contact with no important neurological structures, and since the nerves in the intervertebral spaces are covered with dural sheaths, permanent nerve injury is highly improbable (Fig. 2). If dural puncture should occur, recognition is easy, and spinal anesthesia with an appropriate dose of the anesthetic agent is the worst that can happen to the patient.

Spinal nerve block at the intervertebral foramina outside the dura has been called epidural but in Europe where it steadily grows in favor it is called peridural. Dogliotti[14] has used it more than 25,000 times. Other thousands of cases have been reported.[15] Peridural anesthesia has been selected for cesarean section, however, in comparatively few cases. Crouch and Merry[16] have reported a few cases, Ruppert[17] 103 cases, and Dolff[18] 100 cases. In the United States, Flowers[19] has recorded 37 cases and Moore,[20] 100 cases.

Material

We[21] have already reported 125 cesarean sections performed under continuous lumbar peridural block with procaine and xylocaine.* We now report 121 additional cases with the hope that our satisfaction with this method will encourage others to study its practicability and safety and possibly make contributions to the perfection of its technique.

From 1952 to 1954, 139 cesarean sections were performed in St. Catherine's Hospital by twenty-one operators. All anesthetics were administered by the attending anesthesiologists and their residents. Peridural anesthesia was selected for all but 18 of these patients, who received local or general anesthesia for varying reasons.

The type of operation in the 121 cases performed under peridural anesthesia was: transverse lower segment (113), longitudinal lower segment (4), classical (3), and hysterectomy (1). In every case, abdominal incision was midline below the umbilicus. No preanesthetic drugs were administered to 36 patients. In 58 cases, Demerol, 50 mg., and atropine, 0.0004 mg., were administered and in 19 cases atropine only was given. In the other cases, sedation varied.

The indications for operations were now and then multiple as is so often the case. They are stated in Table I.

Technique for Peridural Anesthesia in Cesarean Section

An intradermal wheal with 2 per cent cyclaine† will determine any rare individual sensitivity. A 16 gauge, Huber-point needle is inserted directly in the midline between the second and third lumbar spinous processes with the bevel upward. With practice, the varying resistance to the plunger of the

*Lidocaine hydrochloride—Astra Pharmaceutical Products, Worcester, Mass.
†Hexylcaine hydrochloride—Sharpe & Dohme, Inc., West Point, Pa.

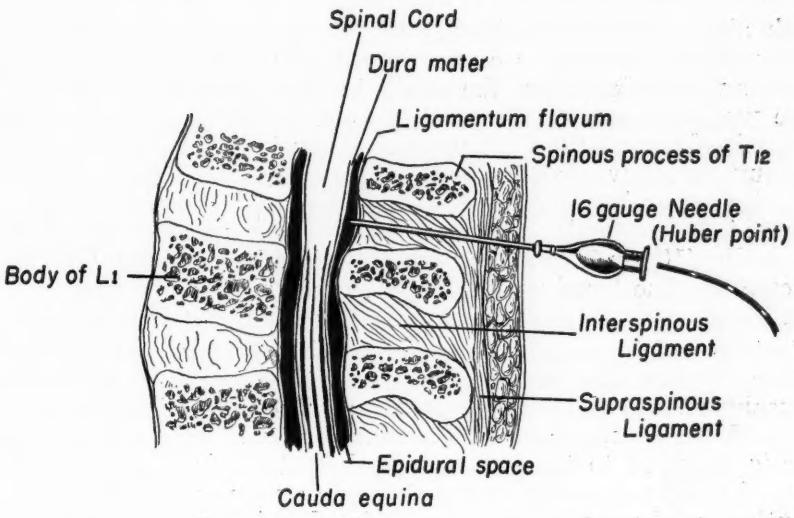

Fig. 3.—The ligaments of the spine and the coverings of the cord. Each spinal ligament has different density, and resistance to injection of air through it is the key to approach to the peridural space. The ligamentum flavum is the most dense and has the greatest resistance. After this ligament is traversed, all resistance ceases, indicating entrance into the peridural space.

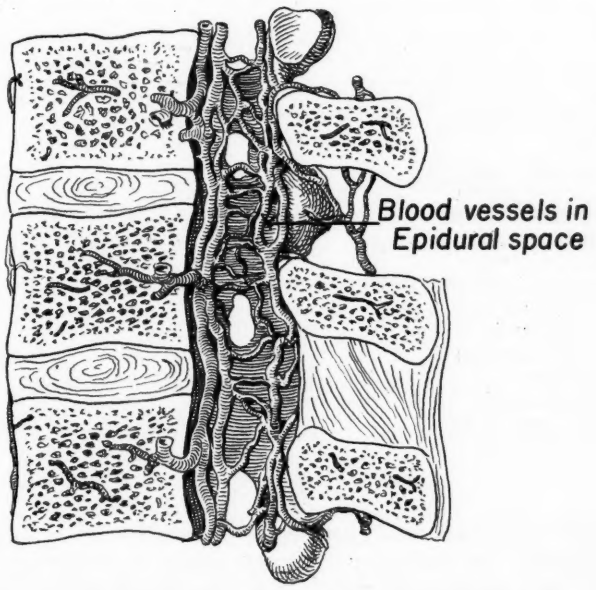

Fig. 4.—Dense vascular plexuses in the peridural space are likely to rupture if traumatized. Toxicity of the anesthetic agent must be low because of rapid absorption from this highly vascular area.

syringe attempting to inject air through the needle as it makes it way through the spinal ligaments—the supraspinous and interspinous ligaments, and the ligamentum flavum—is the key to successful block (Fig. 3).

With almost absolute resistance at the ligamentum flavum the needle is cautiously advanced for 4 to 5 mm. Sudden loss of resistance to pressure of the plunger will indicate that the needle has traversed the yellow ligament and is in the peridural space. Absence of spinal fluid is, of course, essential in ruling out inadvertent dural puncture. If penetration has occurred, the procedure must be converted to continuous spinal anesthesia. Obviously, the amount of anesthesia would not be safe for subarachnoid block. A Tuohy catheter (3.5 F. ureteral), without stylet, is now passed through the length of the needle (10 cm.) following which it is advanced upward for no more than 5 cm., lest fine blood vessels in the peridural space be ruptured (Fig. 4). If frank bleeding should occur, the procedure should be abandoned.

A test dose of 1.5 c.c. of 2 per cent cyclaine (30 mg.) is then administered. From three to five minutes later the patient's legs are tested for numbness, motor weakness, and elevated temperature. The needle is then removed, leaving the catheter in place in the peridural space. The exposed part of the catheter is strapped to the patient's back and she is returned to the supine position. A 17 gauge needle is inserted into a vein for administration of glucose solution and 1 per cent Neo-Synephrine drip is begun slowly.

Once again it is made certain that the patient does not have subarachnoid block. Then, the patient having already received 40 mg. of cyclaine peridurally in the test dose, injection of the anesthetic agent through the catheter is begun. Cyclaine (15 c.c. of 2 per cent) is injected slowly over a period of five to seven minutes. The patient is now ready for operation.

TABLE I. INDICATIONS FOR PERIDURAL ANESTHESIA

INDICATION	NO. OF CASES
Previous cesarean section	62
Disproportion and inertia	17
Elderly primipara	8
Breech	5
Abruptio placentae	3
Placenta previa	5
Myomas	4
Previous pelvic surgery	3
Fetal distress	2
Abnormal presentation	5
Face 1	
Brow 1	
Transverse 1	
Diabetes	3
Pre-eclampsia	3
Rectovaginal fistula	1

Results

There were no maternal deaths or complications. Neonatal death occurred three times. In no case, so far as could be determined, was death due to anesthesia. One fetus with marked hydrocephalus lived but a few minutes; another (1,672 grams), associated with abruptio placentae, died of infectious bronchopneumonia; and the third death, attributed to atelectasis, followed cesarean section on a diabetic mother.

There were no massive spinal anesthesias due to inadvertent puncture of the dura. In three cases, however, which have not been included in this

series, the planned peridural procedure was converted to continuous spinal anesthesia when the dura had been penetrated by the stylet in the catheter. The stylet is no longer used.

In five cases anesthesia was not completely satisfactory, possibly because the anesthetic agent had been deposited in a spinal ligament and not in the peridural space. Local, inhalation, or intravenous anesthesia had to be added.

Sympathetic blockade of necessity accompanies peridural anesthesia; hence, hypotension occurs in every instance. Since the sympathetic block is gradual, however, and segmental, both hypotension and hypertension are easily controlled and of no consequence. Hypotension is never sudden or great as with spinal anesthesia. There were no neurological symptoms, and not a single headache in the entire series.

The anesthetic agent is important. In our first series of 125 cesarean sections, convulsive movements occurred twice in 41 cases in which 2 per cent xylocaine had been used. In this series of 121 cases xylocaine was used in 64 cases and cyclaine in 57 cases. No convulsions were observed. Difference in toxicity of these two anesthetic agents appears to be marked. In a total of 931 peridural and peripheral nerve blocks for general surgery in which 2 per cent xylocaine had been used, convulsions occurred in 10 cases (an incidence of 1.07 per cent) and in 262 cases in which 2 per cent cyclaine was the anesthetic agent, there were no convulsions. In our opinion, cyclaine is the better agent for peridural anesthesia. We now use cyclaine only. It satisfies these requisites for an agent used in peridural anesthesia; namely, (1) low absolute and relative toxicity, (2) high potency, (3) short latent period, (4) prolonged effect, and (5) high diffusability.

Summary

1. One hundred twenty-one cesarean sections under continuous peridural anesthesia are added to 125 previously reported by us.

2. Hypertension is not a contraindication to peridural anesthesia, nor is hypotension, unless due to hemorrhage or shock. Peridural anesthesia should not be elected in any case of severe anemia.

3. The exacting technique required for entering the peridural space should restrict this procedure to the trained anesthesiologist. The comparative simplicity of subarachnoid block is perhaps the principal reason for widespread administration of spinal anesthesia by others.

4. Safety, no neurological sequelae, no spinal shock are obvious advantages of peridural anesthesia.

5. Complete freedom from spinal headache is a comfort for the patient, the obstetrician, and the anesthesiologist.

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32 REMSEN STREET, BROOKLYN
544 EAST 43RD STREET, BROOKLYN

A PRESSURE SYSTEM FOR CONTROL OF POSTPARTUM UTERINE HEMORRHAGE

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(From the Myre Hospital)

ONE of the most distressing problems facing modern physicians is postpartum hemorrhage. While the more serious phase of this complication of pregnancy is infrequent, it is, nevertheless, one of the leading causes, and also an important contributing cause, of maternal mortality, and thus is an ever-present, dangerous possibility.[1]

Of the 3,216 maternal deaths reported in the United States in 1949, 545 were recorded as being due to hemorrhage of pregnancy and childbirth.[2] It is the impression of many modern students of this problem that the percentage of maternal deaths from bleeding is actually increasing.[3, 4, 5] This situation suggests that there may be considerable room for improvement in the management of postpartum hemorrhage.

The accepted treatment of this condition includes inspection of the cervix and birth canal for lacerations, the use of ergonovine or Pitocin, uterine massage, transfusion, bimanual compression of the uterus, uterine packing, and, finally, hysterectomy.[3, 4]

In reviewing the literature on this subject, one is impressed by the lack of really effective nonsurgical treatment for serious postpartum bleeding. One of the most used techniques has been packing the uterus. Numerous authors now feel, however, that uterine packing is not as reliable as had been believed, and numerous reports of women continuing to bleed after packing appear to substantiate this impression.[1, 3, 4]

Many authors feel that, for this reason, hysterectomy should be resorted to earlier, before the patient is in a nearly moribund condition. Cosgrove,[6] for example, reported that in 6 per cent of the fatal cases in his series hysterectomy had been performed as a last resort.

One might feel, therefore, that an effective treatment, less radical than hysterectomy, would have a place in the treatment of postpartum hemorrhage.

There have been a number of nonsurgical procedures devised to save a mother with massive bleeding from shock and death. Some of these include: packing the uterus with Gelfoam,[7] use of an intrauterine balloon,[8] and using a special type of intrauterine pack as a traction device to compress the uterine blood supply.[9] None of these techniques, however, has apparently achieved widespread use.

The technique to be described here has been used successfully to control postpartum hemorrhage over the course of twenty-nine years of active general

practice, in 50 or more cases. It has been employed in cases of bleeding from a variety of causes, including cervical lacerations, where it was deemed expedient to defer more definitive treatment. It has been used in cases of massive postpartum hemorrhage as well as instances of slow, continuous bleeding, and has always been successful in controlling hemorrhage without any detrimental effect on the patient. In cases of bleeding due to uterine atony no further treatment has been needed. In selected cases of retained placental tissue or laceration, temporary effective hemorrhage control has allowed later definitive treatment without any haste or risk of permitting shock to develop.

The importance of immediate control of the hemorrhage can be seen from cases reported where mothers bled to death while attempts to start blood by venipuncture or a cut-down failed.[3]

Method of Applying Pressure System

Two people, each grasping one diagonally opposite corner of an ordinary hospital sheet (preferably one well worn, making it supple), pull the sheet taut and wind it into a ropelike shape by swinging it through a motion like that used in rope skipping.

The center of the ropelike sheet is then placed behind the patient's back in the mid-lumbar region. The ends of the sheet are then brought over the abdomen and a knot tied and tightly drawn down, compressing the abdomen above the uterus. If after a brief wait the knot is retightened, it often increases the constriction of the abdomen. This, then, forms a very tight constriction around the abdomen between the lower ribs and the crest of the ilium. A second knot is then brought down tightly onto the first, making a square knot.

With the use of sterile technique, the largest sized Graves vaginal speculum is inserted deeply into the vagina and opened wide. Two hand towels are then forcefully inserted as high up into the birth canal as possible without any special attempt to pack them into or keep them out of the uterus. One corner of each towel is left out and tagged with forceps (Fig. 1).

The free ends of the constricting sheet are then tied together and connected to traction weights by means of a rope (Fig. 2). The foot of the bed is elevated to counteract the pull of the weights. An assistant may maintain traction manually until the traction apparatus is readied. Fifteen to thirty pounds' traction is used up to twelve or more hours.

Next, a towel, preferably Turkish (less slipping), is wadded up to about the size of a grapefruit and, by means of a temporary release of the traction force, is wedged between the abdominal wall and the encircling sheet, so that the wedge lies cephalad to the center of the uterine fundus (Figs. 3*a* and 4*a*).

It has been our experience that hemostasis is always attained when this wedge is appropriately placed and held in proper position. Maintaining the proper relationship of the wedge to the center of the fundus is somewhat of a balancing act requiring careful, frequent attention at first to avoid an ineffective situation as depicted in Figs. 3*b* and 4*b*. This is particularly important in obese patients on whom it is sometimes necessary to manipulate the wedge constantly until the fundus becomes stabilized. Forces (represented by arrows) acting on the towel wedge are shown in Fig. 3*a:* Arrow I, pressure of abdominal contents forcing wedge anteriorly, Arrow II, pressure of fundus forcing cephalad, Arrow III, vector force of pressure system, forcing wedge posteriorly and caudally. In Figs. 3*b* and 4*b* the system is ineffective. The fundus of the uterus has started to slip around the wedge laterally or posteriorly. If this motion is unchecked the fundus will come to rest in a position

cephalad to the wedge. The femoral arteries are palpated for pulsation and any impairment to the circulation of the lower extremities is corrected by adjusting the towel wedge or reducing traction weight.

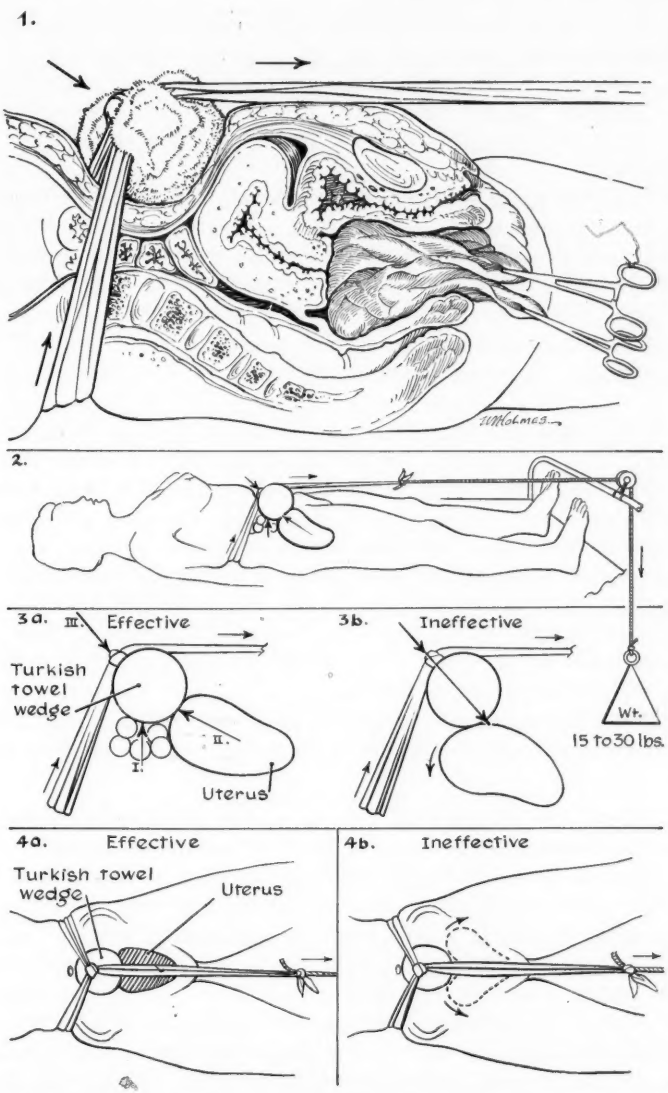

Fig. 1.—Sagittal section showing pressure system in proper position with Turkish towel wedge compressing abdomen and two hand towels in vagina.

Fig. 2.—Demonstrating traction attachment.

Fig. 3*a*.—Sagittal diagram of effective position.

Fig. 3*b*.—Sagittal diagram of ineffective position due to slipping of the fundus of the uterus posteriorly.

Fig. 4*a*.—Front view of effective position.

Fig. 4*b*.—Front view of ineffective position showing fundus of uterus slipping to either side away from the wedge.

Two case reports will illustrate the use of this system.

CASE 1.—A 23-year-old para ii, gravida iii, was admitted in labor on Oct. 13, 1953. Examination revealed a full-term pregnant, white woman with the cervix 4 cm. dilated and in good labor. No abnormalities were found. Routine prepartum work-up had been nega-

tive, the patient giving no history of previous complications of pregnancy or delivery. There was no history of abnormal bleeding or bleeding tendency, and the hemoglobin had been within the normal range. The patient was given 50 mg. of vitamin K on admission and routine predelivery care was administered.

Following six hours of labor an 8 pounds male infant was delivered spontaneously without any complications. The patient had not required any sedation during labor, and open drop ether was given for about two minutes after the head was controlled by the Ritgen maneuver. The placenta was delivered easily by gentle fundal pressure and 1/320 grain of ergonovine was given intramuscularly. Inspection of the placenta showed no abnormality and it appeared intact.

Almost immediately after delivery of the placenta the uterus became markedly atonic and a massive hemorrhage ensued. Ergonovine, 1/320 grain, was given intravenously and gentle uterine massage carried out. Massive bleeding continued, however, and the measured blood loss was over 400 c.c. in less than three minutes. The cervix was inspected and no laceration was seen. Blood was observed pouring from the uterus.

A forceful bimanual compression was immediately carried out, which partially controlled the hemorrhage. This was continued for about 15 minutes while the apparatus was readied.

As soon as the bimanual compression was released profuse bleeding recurred, which was, however, immediately controlled by the application of the system described, using 30 pounds' traction. In this case, because of the absence of obesity, it was necessary to check the position of the wedge about ten times, with adjustments necessary about six times in order to maintain proper relationship of the wedge to the fundus.

The patient's blood pressure and pulse remained normal, and she felt well. The weights were reduced by 5 pounds every half hour. Ten pounds of weight was left on for over twelve hours, after which the entire apparatus, including the vaginal packing, was removed without any resumption of bleeding. The hemoglobin determination repeated twenty-four hours later was still within the normal range.

The patient was given penicillin prophylactically, and had a normal postpartum course. She tolerated the procedure well, and follow-up examination ten days after discharge revealed no abnormality.

CASE 2.—This 29-year-old para iii, gravida v, was seen for the first time on Dec. 17, 1953, after she had experienced about seven hours of unattended labor at home.

Physical examination revealed no significant abnormality, and routine laboratory work was negative. The cervix was dilated about 1.5 cm. and approximately 50 per cent effaced.

Fifty milligrams of vitamin K was given intramuscularly, and the patient prepared for delivery. After another four hours of good labor a 5 pound, 2 ounce, female infant was delivered by the Ritgen maneuver without any difficulty. The patient had received 50 mg. of Demerol two hours before delivery and drop ether during the Ritgen maneuver.

Signs of placental separation were not observed and within five minutes after delivery intense bleeding began. Manual extraction of the placenta was attempted, but was unsuccessful. Because of the difficulty encountered in removing the placenta, and because of the marked bleeding which continued, consultation from a distant town was called immediately.

Intramuscular and intravenous ergonovine, 1/320 grain, had been given as soon as the hemorrhage started but had no observable effect on the bleeding.

In order, therefore, to stop the severe hemorrhage until consultation arrived, the pressure system described above was rapidly applied, requiring only about three minutes. A vaginal speculum was not immediately available so two sterile towels were simply packed well up into the birth canal by hand and tagged with forceps. Proper balance between the Turkish towel wedge and the fundus of the uterus was readily achieved since the patient was quite thin, and bleeding stopped almost immediately. Only 15 pounds of weights was required on the traction apparatus. The patient tolerated the procedure well, except for slight superficial pain in the back where the windlass pressed against her skin.

When the consultant arrived another attempt at manual removal was successful, the placenta being torn into three main fragments. Manual curettage revealed the uterine cavity to be clear.

It was interesting to note that during the second attempt at manual removal of the placenta much less bleeding was encountered than during the first attempt. Duration of the third stage of labor was about 1 hour.

After removal of the placenta, bleeding stopped and it was not necessary to reapply the pressure system. The patient's blood pressure and pulse remained above shock level during the entire procedure despite an estimated total blood loss of 650 c.c. She was given penicillin prophylactically, and had a subsequent normal course.

Summary

The problem of severe postpartum hemorrhage was briefly discussed. An effective nonsurgical method of treatment was described, and two case histories of postpartum hemorrhage presented.

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THE PATHOGENESIS OF PUERPERAL ANURIA AND THE VALUE OF RENAL-ASPIRATION BIOPSY EXAMINATION

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THE renal lesion encountered in this series of patients appears to be the most important of the acute disturbances of the urinary system, not only because of the frequency of its occurrence and the gravity of its ultimate effect, but because of the protean aspect of its origin. The purpose of this report is to review the pathogenesis of puerperal anuria and to demonstrate the value of renal-aspiration biopsy examination. Although the merit of this procedure is somewhat academic at present, it may give indications for future changes in therapy. Except for the work of Iverson and Brun,[1] the literature does not record any detailed study of renal tissue obtained by the needle-aspiration technique. The clinical and pathological features of this form of renal damage have been thoroughly described by many investigators.[2-5]

Material

Fifteen cases of acute renal failure occurred in obstetrical and gynecological patients at our hospital from 1943 to 1952 (Table I). The youngest patient was aged 19 and the oldest aged 40. Parity varied from none to 16 gestations; the median was 2 living infants. Renal-aspiration biopsy examination was performed in Cases 9 and 12. The clinical courses of these two patients are briefly described.

CASE 9.—B. C., a 19-year-old para ii, gravida ii, entered the gynecological service with a diagnosis of septic abortion. Catheterization on admission to the hospital produced 10 c.c. of a burgundy-colored urine. The hemoglobin was 10 Gm. and no evidence of shock was present. The urinary output remained at 100 to 150 c.c. per day for the subsequent nine days. The blood urea became elevated to 310 mg. per cent and the blood creatinine was 20 mg. per cent. The temperature varied from 101 to 104° F. The patient was given antibiotics and packed red blood cells with no untoward reaction. A strict intake-output regimen was maintained. Thirteen days after an adequate urinary output had been established a renal biopsy examination was performed. The patient was discharged on the twenty-sixth hospital day. The blood chemical studies at that time were normal but some residual inability for renal concentration persisted.

CASE 12.—B. A., a 38-year-old para v, gravida v, was referred to the obstetrical service in the thirty-second week of gestation for acute toxemia. The day following therapy with a hypotensive agent, although no marked fall in blood pressure was recorded, oliguria ensued. The blood urea increased to 105 mg. per cent and a dark amber urine was noted. The

Fig. 1.

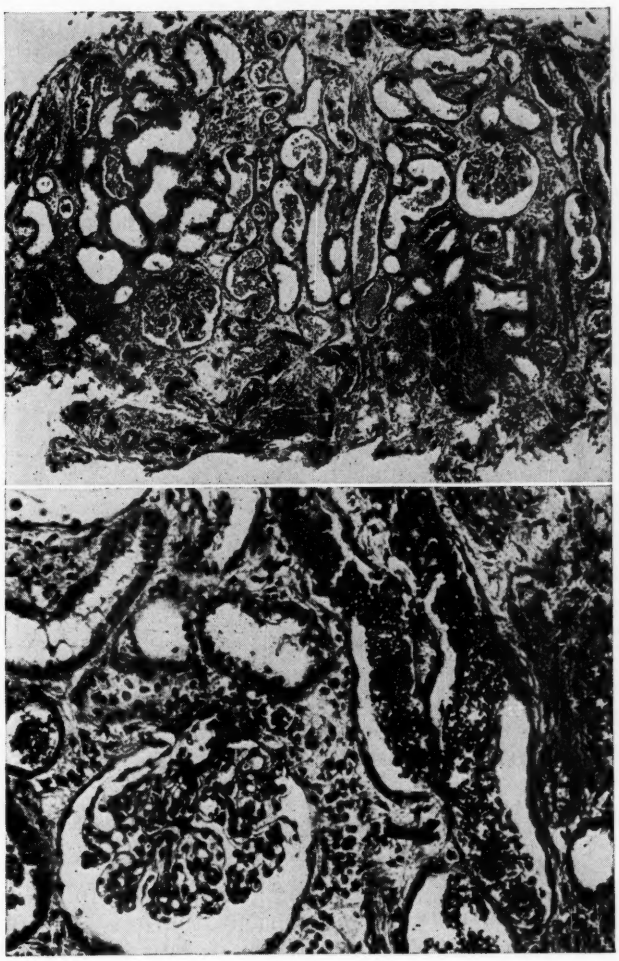

Fig. 2.

Fig. 1.—(Case 9.) Renal biopsy 22 days after the onset of anuria and 13 days after cessation of renal shutdown. Many tubules are filled with solid material in the form of heme casts and debris. (×60; reduced ⅕.)

Fig. 2.—(Case 9.) Swollen vacuolated epithelium in some tubules with moderate interstitial edema and infiltration with monocytes and leukocytes. Basement membrane broken and epithelium disrupted in one area. (×285; reduced ⅕.)

urinary output remained below 300 c.c. for the subsequent 13 days. The patient was delivered of a macerated 2,600 gram infant nine days after the onset of oliguria. A renal-aspiration biopsy examination was made on the tenth day of the urinary suppression. The patient was discharged on the thirty-fifth hospital day in good condition.

Results

Sepsis was present in 6 patients (Cases 1, 4, 8, 9, 11, 14). In one of them (Case 4), however, it was associated with shock. Four of the patients died after 8, 8, 9, and 17 days of urinary suppression during which the blood urea reached 188, 450, 354, and 454 mg. per cent, respectively. In each instance an autopsy was obtained and after pathological examination of the kidneys a diagnosis of "hemoglobinuric" nephrosis was made. Two patients recovered; they had oliguria (excretion of less than 600 c.c. of urine in 24 hours) which lasted ten days. An aspiration renal biopsy examination was performed in Case 9 thirteen days after the diuretic or recovery phase had begun (Figs. 1 and 2).

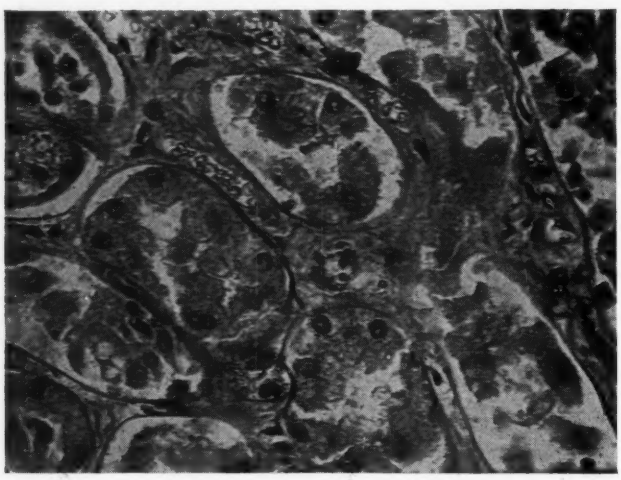

Fig. 3.—(Case 11.) Renal biopsy 10 days after the onset of oliguria and 2 days before the recovery phase began. Disruption of basement membrane in two tubules.

The biopsy technique of Iverson and Brun[1] was followed and in conformity with their experience no complication resulted. The histological sections from Case 9 were reviewed by Professor J. Oliver,[6] who stated that they showed moderate residual renal damage as evidenced by casts and debris in the tubules. Areas where the basement membrane was broken or frayed and the epithelial lining disrupted were present. He also noted a moderate amount of interstitial edema and infiltration with monocytes and leukocytes. This lesion might explain the clinical feature of lack of renal concentration and continued renal insufficiency despite excellent urinary output. Professor H. L. Sheehan[7] agreed that the characteristic appearances of a hemoglobinuric nephrosis in the late stages was present. "The glomeruli show no significant change and the proximals vary; some have a low epithelium of a kidney working under load while others appear to be rather dilated. In addition the distals are plugged by hemoglobin derivitive casts. The more important tubules, the medullary collectings, are not present. A considerable interstitial fibrillary

TABLE I. SUMMARY OF FIFTEEN CASES OF ACUTE RENAL FAILURE

CASE NO.	YEAR	NAME	AGE	ETIOLOGY	DURATION OF RENAL SUPPRESSION	BLOOD UREA (MG. %)	OUTCOME
1	1943	C. A.	26	Septic abortion	8 days	450	Died. Autopsy—"Hemoglobinuric nephrosis"
2	1943	M. C.	29	Abruptio placentae	9 days	200	Lived
3	1949	B. M.	32	Prolonged shock	2 days	90	Died No autopsy
4	1949	A. J.	22	Septic abortion shock	9 days	354	Died Autopsy—"Hemoglobinuric nephrosis"
5	1950	B. C.	24	Transfusion reaction	9 days	240	Died Autopsy—"Hemoglobinuric nephrosis"
6	1951	C. A.	24	Transfusion reaction	12 days	310	Lived
7	1951	B. S.	40	Abruptio placentae	3 days	208	Lived
8	1951	A. A.	40	Septic abortion	16 days	454	Died Autopsy—"Hemoglobinuric nephrosis"
9	1952	B. C.	19	Septic abortion	10 days	310	Lived Renal biopsy
10	1952	K. M.	22	Abruptio placentae	3 days	158	Lived
11	1952	M. N.	29	Septic abortion	10 days	250	Lived
12	1952	E. A.	38	Hypotensive drug Acute toxemia	14 days	105	Lived Renal biopsy
13	1952	I. H.	19	Transfusion reaction	2 days	88	Died Autopsy—"Lower nephron nephrosis"
14	1952	D. G.	29	Septic abortion	8 days	188	Died Autopsy—"Lower nephron nephrosis"
15	1952	C. H.	30	Shock	9 days	142	Lived

edema with a good deal of cellular infiltration with monocytes exists. No recognizable disruption of epithelial lining is seen and the basement membrane appears intact.''

Oliguria was noted in Cases 2, 7, and 10 following abruptio placentae. The period of urinary suppression in these patients lasted 9, 3, and 3 days, respectively, but they recovered. In Sheehan's[8] analysis of 700 cases of abruptio placentae, he noted a greater proclivity for damage to the kidneys in the instances of abruptio which occurred in the earlier months of pregnancy. The earliest case in his series appeared at 24 weeks of gestation while in our group the patients were 31, 32, and 33 weeks pregnant.

Three patients had acute renal failure associated with transfusion reactions. One of these (Case 6) had urinary suppression for 12 days and the blood urea reached 310 mg. per cent before the onset of diuresis. Another (Case 13) died two days following a cesarean section during which an incompatible blood transfusion had been administered. The third patient (Case 5) had a marked oliguria, icterus, mahogany-colored urine and a blood urea of 88 mg. per cent. She survived oliguria for nine days and appeared to be improving. An evisceration occurred. This event, coupled with the diuretic phase of acute renal insufficiency, may have produced sufficient electrolyte imbalance to cause death. Autopsies were performed in Cases 5 and 13 with the anatomical diagnosis of ''hemoglobinuric'' nephrosis submitted.

An instance of acute renal failure in the absence of clinical shock occurred in one patient (Case 15). Twenty-four hours prior to admission she had an estimated blood loss of 1,000 c.c. associated with a threatened abortion but entered the gynecological service afebrile and normotensive. Oliguria followed for nine days with an elevation of the blood urea to 142 mg. per cent before the recovery phase began. Ostensibly the blood loss was sufficient to cause renal ischemia and tubular damage yet only transitory hypotension. The disturbance of the renal circulation is, however, not always a transient process and prolonged ischemia can lead to irreversible protracted renal injury, as illustrated in Case 3. This patient died two days after admission to the hospital, having never completely recovered from severe blood loss and shock despite multiple transfusion. No autopsy was procured.

The combination of acute toxemia and a hypotensive drug appeared to be the underlying cause of renal failure in Case 12. The day following therapy, although no marked fall in blood pressure was recorded, oliguria ensued. A renal-aspiration biopsy examination was made on the tenth day of urinary suppression but no significant pathological findings were noted. The explanation of this apparent lack of correlation between anatomical and functional states may be due to the patchiness of the focal cortical ischemia and consequent tubular damage. Admittedly, however, there was no definite evidence that cortical ischemia actually occurred or that a patchy tubular damage resulted.

The disruption of the epithelial linings and what appear to be breaks in the basement membranes of the tubules are seen in Fig. 3. This is not tubulorrhexis but merely mangling of tissue. Other areas with less surgical trauma did not reveal any abnormal changes. The mortality rate in 15 patients was 46 per cent.

Comment

The renal pathological picture has been called a lower nephron nephrosis by Lucke[3] who from his investigations based on 538 fatal cases concluded that the distal tubule only was affected. The concept of a lesion unique in its localization

to the lower nephrons appears to be no longer valid. Oliver, MacDowell, and Tracy,[4] by the mounting and staining of entire nephrons, have demonstrated that in acute renal failure related to toxic and traumatic injury, the structural alterations which can be correlated with and which may reasonably explain the functional disturbances in the kidney are those of tubular damage. They encountered two sorts of tubular injury, the first a nephrotoxic necrosis limited to that part of the nephron, the proximal convolution, which is functionally concerned with the handling of the poison and, since poisons are distributed by the renal circulation, all nephrons were equally involved. The second type of lesion was a disruption of the renal tubule, tubulorrhexis, which is due to focal cortical ischemia occurring at random in any part of the nephrons. In the reparative process in the kidney of acute renal failure the disruption or dissolution of the basement membrane is a factor which prevents tubular repair. Not only is there no directing surface on which regenerating epithelial cells creep to re-form the tubule but the gap in the tubule is invaded by granulation tissue which fills and obliterates the lumen. They discussed the nature and distribution of tubular lesions, the degree and type of tubular occlusion, emphasized the occurrence of the interstitial reaction, and described the presence and effects of deposits of pigment. In all the kidneys examined, from every clinical variety of the syndrome, the destructive lesion was found by them in every part of the nephron from the periglomerular proximal convolution to the connecting tubules where they join the collecting ducts. Random distribution both in the nephrons and among the nephrons was its characteristic.

Sheehan[7] is of the opinion that the lower nephron nephrosis concept is as valid today as it was twenty years ago. There is a secondary effect on the proximal tubules and the glomeruli just as there is a secondary effect on the structures if the ureter is ligated. In addition, there are late effects on them as part of the repair processes in the kidney as a whole; these are tubulorrhexis lesions that develop in a kidney a week or later after the original damage. It is open to very interesting debate whether one is entitled to invoke focal cortical ischemia when one wants to explain tubulorrhexis, whereas one may infer that the renal circulation goes equally to all nephrons when one explains nephrotoxic necrosis. One of the most significant pieces of evidence which everyone conveniently ignores is that the third stage of postpartum hemorrhage and shock never produces subsequent oliguria unless someone gives an incompatible transfusion.

The importance of septic abortion as a cause of renal damage is vividly emphasized in our series by the fact that four of the seven patients who died had this condition associated with their renal failure. There is no agreement as to the role played by sepsis in the pathogenesis of the renal lesion and this factor is apparently not easy to assess. Infection per se has not been known to produce acute renal failure unless it was associated with the destruction

of tissue, hemolysis of blood, or accompanied by shock. No definite factor has been identified in these cases. Two patients in this group had intrauterine soap injections and one had a *Clostridium welchii* infection. Wyatt and Goldenberg[11] presented a review of the literature on acute renal failure which resulted from septic abortion. They stressed the importance of prompt treatment of the septic abortion per se with antibiotics and blood transfusion as a prophylaxis against postabortal anuria.

The renal damage observed by Sheehan[12] in abruptio placentae was probably minor and had no lasting importance in the vast majority of patients who recovered but even if there were no residual damage the incidence of gross renal pathology in the entire series of patients with abruptio certainly presented a serious problem. He believes the essential renal disturbance in the kidney results from a period of very intense renal arterial spasm which begins about the same time as, or very soon after, the abruptio occurs. The significant effect of the arterial spasm is in its duration and the pathological lesions encountered were ranged in a series of increasing severity corresponding to this duration from Grade I characterized by only proteinuria due to damage of glomerular capillaries to Grade VI which resulted in gross cortical necrosis. Alternatively, Young postulated that the tubular damage of acute renal insufficiency is determined by the toxic action of some material derived from the autolysis of damaged uterine muscle. The blood pigment merely represents the myohemoglobin liberated at the same time as this toxin which is precipitated in the tubules during excretion.[13] There is, however, remarkably little damage to uterine muscle itself, though, of course, hemorrhages do occur.

The mechanism involved in the production of renal failure which follows the administration of incompatible whole blood has been somewhat clarified by recent experimental studies. Yuile, Gold, and Hinds[14] noted that the precipitation of hemoglobin in renal tubules was not entirely dependent upon the acidity or alkalinity of the urine but upon some functional abnormality of nephrons. They emphasized that the ultimate outcome in any given case, both anatomical and functional, is dependent upon a fine balance struck between the degree of renal injury, the level of hemoglobinemia, and the pH of the urine. Readily reproducible pathological lesions closely resembling that of the "transfusion kidney" were obtained by the injection of hemoglobin into rabbits having acid urine, whose renal tubules had previously been damaged to a moderate degree by a short period of complete ischemia or the administration of specific chemical poisons. This seems to support the view that third-stage or postpartum hemorrhage and shock never produce subsequent oliguria unless someone gives an incompatible transfusion.[7]

Traumatic and toxic injury may lead to circulatory insufficiency as a primary event, which causes axotemia through the reduction of renal function.

This insufficiency has been designated as extrarenal or prerenal in character in the sense that by rectification of the extrarenal disturbance and a resulting relief of the renal insufficiency the process may be reversed. Experimental evidence cited by Smith[9] indicates that the urinary changes in shock, namely, oliguria and impaired concentrating power, are due to renal ischemia. The oliguria may be due in part to back diffusion of water through injured tubules which have lost the normal tubular reabsorptive or excretory ability.

The oliguria of toxemia, which occurs in 75 to 85 per cent of severely pre-eclamptic and eclamptic patients, is not yet fully understood. Dieckmann[15] believes that there is spasm of the renal arterioles and capillaries, similar to that seen in the eye and cutaneous vessels. Suppression of urine is due to a lack of glomerular filtration. Renal-aspiration biopsy could prove very useful in these cases.

In the management of acute renal insufficiency conservative therapy produced best results. In obstetrics one should have an awareness, in the antepartum, intrapartum, and postpartum phases, of the consequences of hemorrhagic shock and, in the postpartum and postabortal phases, of the results of prolonged sepsis. Blood and antibiotics given promptly are most valuable. Extreme caution in the administration of fluids is important. It is now widely recognized that the mistake in the past of overzealous administration of fluids, on the theory that the anuric patient was dehydrated, resulted in many deaths from pulmonary edema.[5] In simple dehydration without renal injury the output is usually from 500 to 700 c.c. per day and the urine is highly concentrated in contrast to the severe oliguria and fixed specific gravity of acute renal failure.

Summary

1. The pathogenesis of acute renal failure in septic abortion, in abruptio placentae, in transfusion reaction from incompatible blood, in shock, and in toxemia was reviewed.

2. The value of renal-aspiration biopsy examination in puerperal anuria was discussed.

We are indebted to Professor J. Oliver and to Professor H. L. Sheehan for their critical and constructive review of this paper.

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EFFECT OF SUPINE POSITION ON URINARY OUTPUT IN PREGNANCY

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AS LONG as oliguria and anuria are presenting threats in the toxemias of pregnancy, the obstetrician-gynecologist must be vitally interested in the various factors which influence and control urinary output. The investigations of the past decade reported in the obstetric literature attest the importance of an understanding of these factors. The diuretic or antidiuretic impact of exogenous drugs has been reported[1-5]; endogenous antidiuretic substances have been studied[6, 7]; and a voluminous literature has appeared concerning the influence of sodium, potassium, and fluid intake.[8-11] Despite this wealth of material dealing with the effect on urinary output of factors which are mediated through metabolic substances, intensive investigations have not been recorded dealing with the physical factors which contribute to the maintenance of urinary output.

The present paper reports a series of fundamental investigations concerned with the type and nature of the physical and mechanical influences which govern the output of urine during the last trimester of pregnancy. Predominantly the writers have been interested in the effect of the position of the patient, alterations in intra-abdominal pressure, and the possible effect of ureteral compression by the expanding uterus.

It is interesting to note, in surveying the literature related to this subject, that most of it deals with the physical changes which have been observed, without comment on, or investigation of, the possibility of resultant changes in function. The dilatation of the ureter during pregnancy has long been noted[12] and Parks[13] has recently postulated a mechanical explanation for this phenomenon. Kantor, Jarrell, and Dunlap[14] have discussed the changes in bladder position during pregnancy and labor. In none of these comments, however, has the principal interest been in the effect on excretory rate of the observed alterations.

On the other hand, in 1947 Bradley and Bradley[15] reported that placing a large inflated balloon under a tight binder on the abdomen would produce marked changes in the urinary-excretion rate. They pointed out that under such circumstances a change in pressure on the subject's abdomen would produce rather sharp changes in the amount of urine excreted despite a constant fluid intake. It was suggested by these authors that this change was caused by alterations in pressure on the renal veins, and, actually, moderate changes in renal venous pressure are known in experimental animals to produce marked changes in urine volume and urine composition.[16]

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In spite of the obvious application to the pregnant woman of these experiments, they have remained unconfirmed, and to date no studies have been reported concerned with the effects of pressure or of changes in position on the urinary output in the last trimester of pregnancy. For this reason the experiments here reported were undertaken to determine the mechanical effects of the growing uterus on urinary output and function.

Study No. 1.—

In this study the urinary output of the subjects, all normal women in the last trimester of pregnancy, was determined with the patients lying on their backs and again with the patients lying on their sides. Standard conditions were maintained by performing the test in a fasting state, for a constant length of time (3 hours), and with a constant intake (200 c.c. of tap water orally at the start of the test and 400 c.c. of intravenous 5 per cent glucose administered at a standard rate during the first hour). The bladder was carefully emptied by catheter at the start of the procedure, and all specimens obtained every hour by indwelling catheter. The patient was instructed to lie in the same position either flat on the back or on one side for the duration of the test, and only one of these positions was tested on any given day. The sequence of the tests was altered, so that all subjects did not have the side position tested on the first day or vice versa.

Results.—Thirty-six tests (18 complete sets) were carried out on 10 patients in late pregnancy, and the results are indicated in Table I. From this it can readily be seen that under standard conditions of intake there is a marked difference in urinary output over a short period of time in the last trimester of pregnancy dependent entirely on the change in position of the patient. The total output for the three-hour test period was 105 per cent greater if the patient lay on her side rather than on her back! This observation was consistent among the entire group, and the differences are great enough to be of significance.

TABLE I. THE URINARY OUTPUT OF PATIENTS IN THE LAST TRIMESTER OF PREGNANCY IN THE THREE-HOUR TEST

PATIENT	OUTPUT LYING ON BACK (C.C.)	OUTPUT LYING ON SIDE (C.C.)
AS	158	304
AS	286	255
AS	223	350
OMP	171	635
OMP	111	177
OMP	139	226
OMP	187	225
OMP	234	304
GW	405	604
RK	530	805
PT	454	589
ED	121	339
JK	147	456
JK	124	469
JK	91	542
PR	100	731
JL	238	434
CJ	230	665
Total	3,949	8,110
Output ratio		
Side 2.05 / Back 1		

Comment.—This rather startling result confirms the observations of the Bradleys with respect to a large balloon inflated under an abdominal binder, and would tend to indicate that the physical position assumed by a woman during the last trimester of her pregnancy can promote or inhibit diuresis.

There is nothing in this rather simple single experiment, however, that proves in any way that this is a mechanical effect of the gravid uterus. All of the subjects in this initial study were pregnant, and a nonmechanical or even hormonal influence of pregnancy cannot be ruled out. Remote as such possibilities may be, it seemed wise as a second step to eliminate them.

Study No. 2.—

The same excretion measurements were made under similar conditions and with the identical positions and intake. In this study, however, not all of the patients were pregnant; part of the group selected were suffering from large masses of fibroids. Furthermore, in the present instance the tests were run in duplicate, and in one of the "runs" a tight abdominal binder was applied to the abdomen over the tumor mass, whether a fibroid uterus or a gravid uterus. As a further check, control studies were run on a group of nonpregnant patients without tumors and also on a group of postpartum patients (Table II).

TABLE II. ABSENCE OF ANY CONSISTENT RELATIONSHIP IN CONTROL GROUPS IN THREE-HOUR TEST

INITIALS	ON BACK (C.C.)	ON SIDE (C.C.)
Nonpregnant, Nontumor Patients.—		
A. Th.	792	248
A. Te.	604	370
I. M.	745	727
P. U.	327	385
	2,468	1,730
Postpartum Patients.—		
M. H.	591	619
A. R.	670	520
F. G.	491	702
M. M.	729	477
G. G.	264	694
B. J. H.	733	802
O. M. P.	1,176	561
M. B.	525	573
M. B.	520	584
	5,699	5,532

Results.—Three patients were tested by the abdominal binder technique, one of them being tested twice. As can be seen in the results summarized in Table III, the nonpregnant patient with a pelvic tumor may show the same increase in urinary excretion when she lies on her side as does the pregnant patient. A hormonal influence peculiar to pregnancy does not seem to be a factor in this phenomenon. The point of greatest interest in these results, however, is the fact that when the abdominal binder is tightly applied, there is little increase in urinary output when the patient turns on her side, but there is a marked additional decrease in urinary output produced by applying the binder when the patient is on her back. In other words, whether it be a massive group of fibroids or a pregnant uterus, it would seem impossible to apply sufficient pressure against the pelvic brim to change significantly the output of the patient on her side; but with the patient on her back, a further increase in pressure against the pelvic brim will strongly accentuate the temporary oliguria.

TABLE III. THE ACCENTUATING EFFECT OF A TIGHT ABDOMINAL BINDER OVER A TUMOR MASS IN A MISCELLANEOUS GROUP OF PATIENTS

INITIAL	CONDITION	BACK WITHOUT BINDER (C.C.)	BACK WITH BINDER (C.C.)	SIDE WITHOUT BINDER (C.C.)	SIDE WITH BINDER (C.C.)
R. E.	Fibroid	726	299		443
M. C.	Fibroid	240	270		401
J. K.	Late pregnancy	147	50	456	470
J. K.	Late pregnancy	124	86	469	343

The control groups—both the nonpregnant and the postpartum—showed wide variation in output in the two positions. There was no consistent difference of output in either position. In the postpartum group, the fact that these determinations were made during the first postpartum week (and thus during a period of physiologic diuresis) makes the interpretation of these results hazardous. It appears, though, that the postpartum patient, like the patients in the nonpregnant group, presents no evidence of ureteral compression.

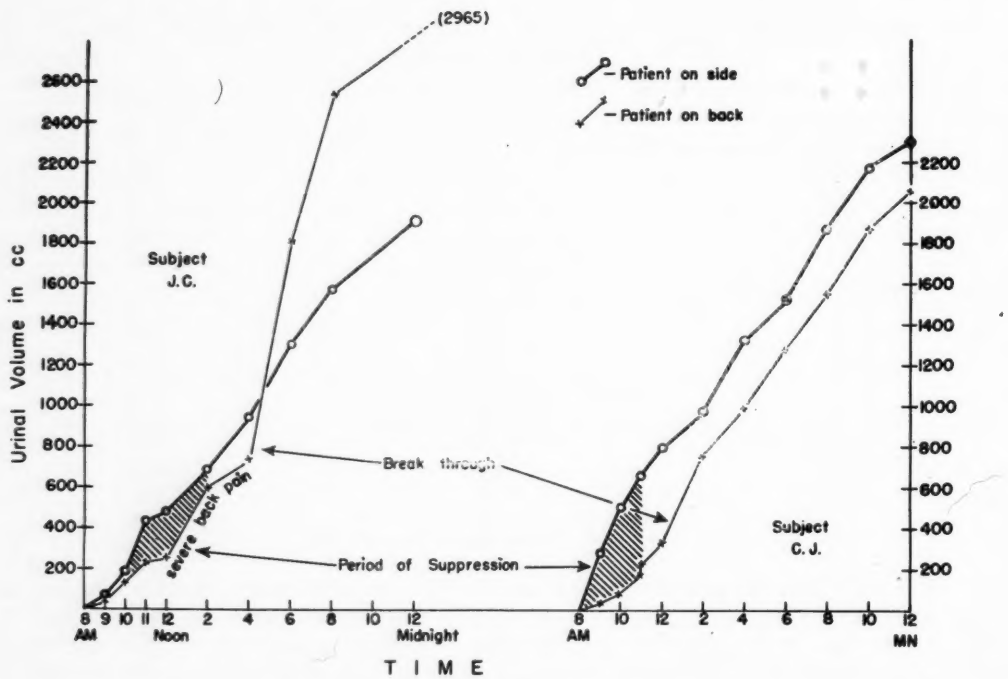

Fig. 1.—Sixteen-hour urinary output tests.

Comment.—These findings seem to point entirely toward a pressure phenomenon. They raise an interesting question, however, as to what becomes of the urine which the patient lying on her back does not void? In other words, does the average pregnant patient have an adequate output only because of occasional random shifts of position? If these results were entirely a reflection of ureteral compression, the urine must be stored in the renal pelvis for the duration of the test, and the differences in elimination would be a phenomenon of the lower tract entirely.

Study No. 3.—

Two volunteers were found who would maintain the same position—either on the back or the side—for 16 consecutive hours, and a similar test was carried out with a controlled fluid intake during this period. Fig. 1 indicates the results. While the output for the first few hours demonstrates the marked difference between the back and the side positions, there is ultimately a "breakthrough" which brings the output in the back position within the range of that in the side position. Presumably the pressure within the renal pelvis rises above that which blocks the ureter, and position becomes less of a factor than intrarenal pressure. It should be noted that in the three hours prior to the "breakthrough" one of the patients (J. L.) complained bitterly of backache, a complaint she did not have while executing the test lying on her side.

Comment.—This study would indicate that position does not cause a true oliguria. Apparently the amount filtered for any period of time is the same, the differences indicated in Study No. 1 reflecting only a difference in the amount which reaches the bladder. This would imply that those determinations which are concerned only with long-range urinary volume should be unaffected by positional changes.

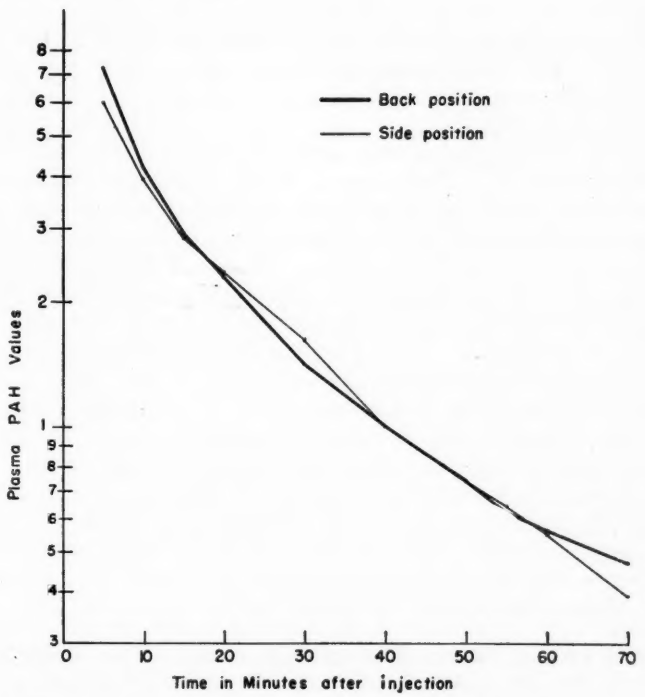

Fig. 2.—Plasma PAH values, plotted in milligrams per cent remaining up to 70 minutes post injection (semilog).*

Study No. 4.—

Mannitol glomerular filtration rates according to the method of Dominguez, Corcoran, and Page[17] were determined with the patients—pregnant and

*Note that during the first 15 minutes after injection the values deviate from a straight-line decay curve, due to initial mixing phenomena. The significant part of the graph, however, starts after mixing is practically completed, and approximates a straight line which is not far from identical in both side and back positions. These values represent the mean from 6 sets of PAH determinations carried out on 6 patients in late pregnancy.

in the last trimester—first on the side and then on the back. There were no significant differences in the glomerular filtration rates in the two positions (Table IV).

Comment.—These findings confirm the conclusion that the changes observed in Studies No. 1 and No. 2 are in response to alterations in position and abdominal pressure. They are not in accord with the suggestion of Bradley and Bradley that all observed alterations in excretion arise from renal circulatory changes; but point rather (as does Study No. 3) to a distal—probably ureteral—influence.

TABLE IV. MANNITOL GLOMERULAR FILTRATION RATE, COMPARING THE SIDE AND BACK POSITIONS

SUBJECT		GFR, BACK POSITION (ML./MIN.)	GFR, SIDE POSITION (ML./MIN.)
H. I.	(8½ months pregnant) 63 kilograms	95	92
M. A.	(8 months pregnant) 110 kilograms	163	152
D. A.	(Control: nonpregnant) 55 kilograms	118	117

Study No. 5.—

Para-aminohippurate clearances were employed for the purpose of comparing renal blood flow in various positions. A method was needed which would not require the securing of frequent voided urine specimens, because the apparent temporary suppression in urinary output in the pregnant patient on her back would render inaccurate any urinary determinations made with the patient in that position. Therefore a single-injection technique was used. Five cubic centimeters of 20 per cent sodium parahippurate was given rapidly intravenously, and blood samples withdrawn from the opposite arm at stated 5 to 10 minute intervals for 70 minutes. Plasma PAH levels were then determined according to the method of H. W. Smith and associates.[18] Six patients in late pregnancy were tested in both the supine and side positions.

Results.—There was found to be surprising agreement between the decay curves, whether the patient was on her side or on her back. Fig. 2 shows decay curves constructed from the means of all the plasma values in the side and back positions, respectively. Table V indicates a fairly consistent relationship between both positions along the curve of individuals tested when expressed as a ratio of 20 minute levels to 40 minute levels, and 40 minute levels to 60 minute levels, respectively. While it is agreed that the use of the single-injection technique will not determine accurately the renal plasma flow in cubic centimeters per minute,[19] this method may still be used for comparison of renal plama flow in the two positions.[20]

TABLE V. THE RATIO OF THE TWENTY MINUTE PAH LEVEL TO THE FORTY MINUTE LEVEL, AND OF THE FORTY MINUTE LEVEL TO THE SIXTY MINUTE LEVEL

SUBJECT	$\frac{PAH_{20}}{PAH_{40}}$		$\frac{PAH_{40}}{PAH_{60}}$	
	ON SIDE	ON BACK	ON SIDE	ON BACK
E. B.	2.30	2.44	1.76	1.98
E. L.	2.14	2.22	1.98	1.85
M. G.	3.36	2.53	1.88	1.88
M. C.	2.20	2.16	1.75	1.58

Comment.—This study is interpreted as indicating that some of the effect on urinary output of the gravid uterus with the patient in the supine position

maybe distal to the renal circulation. Ureteral pressure changes involving less than 20 mm. Hg are known not to affect significantly either glomerular filtration or tubular function.[21]

Summary

The impact on urinary output of changes in intra-abdominal pressure, and hence of venous flow, is a subject of obvious importance. It has interested a variety of workers with a variety of results. The application of such observations to the expanding human uterus during pregnancy has remained uninvestigated, however.

Bradley and Bradley, using a large balloon inflated under a tight abdominal binder, indicated that under such circumstances changes in the position of the patient markedly altered urinary output, and maintained from their studies that these alterations resulted from changes in renal blood flow. Reinhardt[22] applied clamps to the vena cava in the rat and followed urinary output, concluding that the relative oliguria which might be observed was independent of venous congestion. Franklin,[23] following renal blood flow while the uterus of the rabbit was artificially distended with blood or saline, came to the conclusion that the changes noted were based on a uterorenal reflex, or perhaps a hormonal change.

The present studies do not pretend to resolve these conflicting findings in any final sense. The urinary output of the pregnant woman in the last trimester was observed under standard conditions, with only the patient's position altered in the various experiments. These studies indicate that initially the urinary output of the pregnant patient is definitely diminished when that patient lies on her back in contrast to lying on her side. Glomerular filtration rates and renal blood flow studies do not show the same contrast between the supine and side positions, and these together with the other studies here reported point toward a mechanical obstructive influence at or below the pelvic brim.

In this connection it is of interest to recall the studies of Howard, Goodson, and Mengert.[24] These authors, investigating the hypotensive syndrome in the supine patient, found that the increased femoral venous pressure of late pregnancy was a phenomenon observable only with the patient on her back. With the patient on her side, the femoral venous pressure was not significantly altered. Their study and that of McRoberts,[25] as well as the one reported here, indicate a mechanical compression by the expanding uterus which may have marked effects on the function of the adjacent pelvic structures, and which can be largely alleviated by placing the patient on her side.

Conclusions

1. The urinary excretion of a pregnant patient in the last trimester given a standard amount of water is considerably greater with the patient on her side than on her back.

2. This phenomenon can be reduplicated with some large pelvic tumors. The application of a tight abdominal binder, however, which sustains the pressure against the pelvic brim regardless of position does away with the increased output when the patient lies on her side.

3. Glomerular filtration rate determinations and renal blood flow studies indicate that these factors do not alter with alterations in position.

4. Prolonged studies (i.e., sixteen hours) in one position indicate that ultimately the suppressed urine "breaks through," no matter which position the patient maintains.

5. It is felt that at least some of these phenomena are the result of mechanical ureteral pressure, and may represent a functional counterpart of the ureteral dilatation observed during late pregnancy.

We wish to express appreciation to Dr. Leo Sapirstein for his advice and assistance in the preparation of this paper, and also to Mrs. Ruth Greene and Mrs. Alberta Daniel for their aid in carrying out procedures.

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SUPPORTIVE CARE, INTERRUPTION OF PREGNANCY, AND MITRAL VALVULOTOMY IN THE MANAGEMENT OF MITRAL STENOSIS COMPLICATING PREGNANCY*

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ORGANIC heart disease has been diagnosed in 2,932 (3.7 per cent) of the 78,527 pregnant patients at the New York Lying-In Hospital from Sept. 1, 1932, through Dec. 31, 1953 (Table I). Improvements in obstetric care and the availability of blood and antibiotics have reduced the ravages of toxemia, hemorrhage, and infection, so that today cardiac disease is the single greatest cause of maternal mortality at this institution (Table II). There have been 29 deaths in the 2,932 patients with heart disease, a mortality rate of 1 per cent (Table III). Twenty-three per cent of all maternal deaths have been due to heart disease.

TABLE I. INCIDENCE OF PREGNANCY COMPLICATED BY HEART DISEASE

Pregnancies, 1932 through 1953	78,527	
Pregnancies with organic heart disease	2,932	3.7%
Pregnancies with rheumatic heart disease	2,718	3.4%

TABLE II. CHANGING CAUSES OF MATERNAL DEATHS IN ORDER OF MAGNITUDE, NEW YORK LYING-IN HOSPITAL SEPT. 1, 1932, TO DEC. 31, 1953

1932-1937	1938-1942	1943-1947	1948-1953
Infection	Infection	Cancer	Heart disease
Hemorrhage	Embolus	Hemorrhage	Cancer
Pneumonia	Hemorrhage	Heart disease	Infection
Heart disease	Heart disease	Cerebrovascular accident	Toxemia
Embolus	Toxemia	Embolus	
Toxemia	Cerebrovascular accident		
Cerebrovascular accident		Infection	
Cancer		Pneumonia	

TABLE III. MATERNAL DEATHS IN HEART DISEASE

Deaths in 2,932 patients		29	1.0%
Deaths from heart disease		26	0.9%
Rheumatic	20		
Hypertensive	3		
Myocardial	2		
Congenital	1		
Other deaths (noncardiac)		3	0.1%

*Presented at a meeting of the New York Obstetrical Society, March 9, 1954.

Clinical experience and laboratory investigations[1, 2, 3] have indicated there is a predictable hemodynamic burden of pregnancy which starts early in the second trimester, rises to a peak in the third trimester, and returns to or near normal at term. The burden rises again during labor and immediately post partum but usually to a much lesser degree than previously. The antepartum increase in cardiac work is largely due to rises in cardiac output (25 to 50 per cent), blood volume (20 to 40 per cent), and oxygen consumption (5 to 25 per cent). Other physiologic changes in the circulation during pregnancy include: hemodilution, decreased arteriovenous oxygen difference, increased velocity of blood flow, increased heart rate, increased sedimentation rate, leukocytosis, increased venous pressure in the lower extremities, edema, superficial vein dilatation, increased lung markings, changes in the shape of the heart, development of systolic murmurs and third heart sounds, accentuation of the second pulmonic sound, presence of transient basilar râles, development of a capillary pulse, and changes in the electrocardiogram. A knowledge of these physiological changes will eliminate false diagnoses of organic heart disease. The role of the placenta as an arteriovenous fistula, sodium and water balance and their relation to hormonal levels must all be considered in explaining the hemodynamic variations. The bearing-down efforts of the second stage of labor account for the greatest share of intrapartum work. Removal of the placental shunt further augments the burden post partum.

TABLE IV. ETIOLOGICAL CLASSIFICATION OF HEART DISEASE

HEART DISEASE	NO. OF CASES
Rheumatic	2,718
Congenital	87
Hypertensive	72
Arrhythmia	30
Kyphoscoliotic	10
Coronary	5
Myocardial	4
Thyroid	3
Syphilitic	2
Constrictive pericarditis	1
Total	2,932

Table IV shows that approximately 90 per cent of cardiac disease at the Lying-In Hospital is of rheumatic etiology (2,718 out of 2,932 cases of heart disease) and nearly 75 per cent of these patients have mitral stenosis. Eighty-eight per cent of the patients fall into the favorable Class 1 and Class 2 of the New York Heart Association (Table V) and the vast majority of these tolerate the predictable and unpredictable burdens of pregnancy without serious difficulty. Only 12 per cent fall into the unfavorable Class 3 and Class 4 groups yet this relatively small number account for most of the maternal mortality.

In mitral stenosis the opening between the left auricle and left ventricle is narrowed and maintenance or increase of blood flow from auricle to ventricle requires increased left auricular pressure. This increased pressure is reflected in the pulmonary veins, pulmonary capillaries, pulmonary artery

and right ventricle, and ultimately leads to pulmonary edema. The problem of severe mitral stenosis in pregnancy may be approached from five different aspects:

1. Reduce the predictable burden of pregnancy.

Clinical and laboratory studies indicate there is at present no known way to accomplish this end.

2. Reduce and avoid the unpredictable burdens of pregnancy: overactivity, infection, overweight, anemia, and intravenous therapy of volumetric proportions (Table VI).

TABLE V. FUNCTIONAL CLASSIFICATION IN PREGNANCY COMPLICATED BY RHEUMATIC HEART DISEASE

CLASS	NO. OF CASES	PER CENT
1	1,304	48
2	1,107	40
3	211	8
4	96	4

TABLE VI. UNPREDICTABLE FACTORS IN ANTEPARTUM CARDIAC FAILURE

Respiratory infection	44
Obesity	5
Anemia	2
Pyeloureteritis	2
Transfusion, infusion	2
Coitus	2
Total	57

The dangers of overactivity (physical, emotional, and sexual) are stressed. Hospital care and antibiotics are mandatory in the event of infection, particularly those of a respiratory nature. Weight is controlled by calorie, fluid, and sodium restrictions. Anemia is treated but whole blood transfusions are avoided. Massive infusions are similarly omitted.

3. Remove the cause of the predictable burden by interruption of pregnancy where indicated, feasible, and acceptable.

4. Improve the heart's ability to withstand predictable and unpredictable burdens of pregnancy. In the past this has been accomplished indirectly with supportive therapy but recently a direct approach has been offered by mitral valvulotomy.

5. Discount the burdens of pregnancy by devious statistical analysis.

Statistics[4, 5, 6] have indicated that the average age at death of men and women (nulliparous and parous) with rheumatic heart disease is identical. From these data it has been concluded that maternal deaths from rheumatic heart disease are due to the natural course of cardiac disease and that circulatory burdens imposed upon a woman by the pregnant state are no greater than other burdens she might normally encounter during a comparable nine-month span of time in the nongravid state. This is indeed a dubious approach to the problem. One might just as easily conclude from the same statistics that prostatic carcinoma is never fatal in rheumatic males. In order to evaluate logically the relation of pregnancy to death it is essential that fatalities from heart disease be carefully analyzed rather than summarily disregarded. If

maternal deaths represent the natural evolution of rheumatic heart disease, the fatal cases should be evenly distributed throughout pregnancy. Experience at the New York Lying-In Hospital and most large clinics throughout the country, however, clearly indicates that the onset of decompensation and time of death can be definitely related to the degree of predictable hemodynamic burden. Table VII shows that the antepartum hemodynamic burden remains the most important primary cause of cardiac failure and death. Subacute bacterial endocarditis is now amenable to antibiotic therapy, anticoagulant drugs have decreased the incidence of embolic accidents, deaths due to postpartum hemorrhage are less frequent, and radical obstetrical surgery is no longer employed on cardiac indications. There is a 20 per cent mortality associated with cardiac failure (Table VIII). Table IX shows that cardiac failure occurs most commonly ante partum. Table X shows the relation of antepartum decompensation to the month of pregnancy, the largest incidence of failure corresponding to the time of greatest cardiac burden. Table XI shows a similar distribution of antepartum deaths.

TABLE VII. MATERNAL MORTALITY AND CARDIAC FAILURE IN RHEUMATIC HEART DISEASE

	TOTAL DEATHS	DEATHS DUE TO CONGESTIVE FAILURE
Antepartum	11*	10
Intrapartum	0	0
Postpartum	11†	3‡

*One death was due to acute endocarditis and thrombosis of superior sagittal sinus.
†Two deaths were due to postpartum hemorrhage.
Three deaths followed multiple emboli prior to availability of anticoagulant drugs.
Three deaths were due to subacute bacterial endocarditis prior to availability of antibiotics.
‡Three deaths followed ill-advised obstetrical procedures previously thought to be in the best interest of the cardiac condition: cesarean section 2, version 1.

TABLE VIII. MATERNAL MORTALITY IN RHEUMATIC HEART DISEASE WITH CARDIAC FAILURE

Cardiac failure	96
Deaths due to cardiac failure	19
Mortality in cardiac failure	20%

TABLE IX. ONSET OF CARDIAC FAILURE IN RHEUMATIC HEART DISEASE DURING PREGNANCY

ONSET	NO. OF CASES
Antepartum	82
Intrapartum	5
Postpartum	9
Total	96

Gorenberg and Chesley[7] report only 2 deaths (0.40 per cent) during the fifteen-year period from 1939 to 1953 in over 500 "consecutive" pregnant rheumatic cardiac patients treated at the Margaret Hague Maternity Center with supportive measures alone. The authors conclude that, "Practically every pregnancy encountered in a patient with rheumatic heart disease can be brought to a successful termination," and that, "The burden of pregnancy is not to be feared." Therapeutic abortion is considered unnecessary. Yet

Connell[8] in less than half this fifteen-year period (1944 through 1950) reported 17 deaths (4.9 per cent) from the same institution in some 350 pregnant rheumatic cardiac patients. Gorenberg and Chesley's "consecutive" series excluded all deaths in patients not personally supervised by the senior author either because of his four-year absence from the hospital while in military service or because of indifference to his rules on the part of the private physician. Had these additional 15 deaths been carefully documented, the relation of circulatory burden to cardiac failure and death might have been most instructive. They are no less dead than all of our 20 rheumatic cardiac patients and we have included *all* fatalities, nonregistered and private, yet our mortality rate is only 0.74 per cent. The patient with acute appendicitis who dies of peritonitis following an ill-advised enema and rupture is not excluded from the mortality figures of appendicitis. Sooner or later rules are always broken and no one clinician can be the constant cardiac policeman. Gorenberg's rule, "Admit all Class 3 patients on sight and maintain them on absolute bed rest for the remainder of pregnancy," is frequently impracticable or impossible to enforce, desirable as it may be in selected case.

TABLE X. ANTEPARTUM CARDIAC FAILURE IN RHEUMATIC HEART DISEASE ACCORDING TO MONTH OF PREGNANCY

MONTH	NO. OF CASES
1	0
2	0
3	2
4	7
5	18
6	20
7	21
8	12
9	2
Total	82

TABLE XI. ANTEPARTUM DEATHS DUE TO CARDIAC FAILURE IN RHEUMATIC HEART DISEASE ACCORDING TO MONTH OF PREGNANCY

MONTH	DEATHS
1	0
2	0
3	1
4	0
5	3
6	2
7	2
8	2
9	0
Total	10

We would scarcely deny that rest and supportive measures such as digitalis and mercurial diuretics will improve the ability of the myocardium to withstand extra work and suffice to carry most patients with mitral stenosis through pregnancy successfully. In fact we manage the majority of our severe cases of heart disease in precisely such a manner but we firmly disagree that this method is a panacea. We have had 7 deaths in patients on

absolute bed rest as prescribed by Gorenberg and Chesley and we continue to dread the circulatory burden of pregnancy in advanced mitral stenosis. There are those patients whose mitral valve is so tight and whose cardiac reserve is so severely compromised that no amount of supportive therapy, ideal as it may be with adherence to all the rules, will compensate for the load of pregnancy, particularly hypervolemia. This gestatory increase in blood volume undoubtedly explains the frequency with which pulmonary edema appears for the first time during a pregnancy. Other patients will succumb if supportive measures are the slightest degree short of ideal.

Gorenberg and Chesley state they have carried patients through pregnancy whose previous pregnancies had been interrupted elsewhere. We have had similar experiences. Patients are not infrequently subjected to laparotomy for acute appendicitis and prove to have a ruptured Graafian follicle. Others with acute appendicitis survive with icecap therapy alone. One does not conclude that appendectomy is never indicated or that a medical regimen is preferable. We believe the management of patients with severe mitral stenosis requires the most careful type of appraisal and individualization. No single approach is applicable in all cases: Where supportive therapy cannot completely answer the problem, interruption of pregnancy and/or mitral valvulotomy must be considered.

Gorenberg and Chesley offer other statistics which purport to indicate that longevity is greatest in the patients with the most severe heart disease who bear the largest number of children. Such figures vitiate all clinical experience and their validity is open to question. We do agree there is no evidence to indicate that childbearing shortens life expectancy in rheumatic heart disease *provided* the patient survives the hemodynamic burden of pregnancy. Although the long-term results of mitral valvulotomy are still to be forthcoming, evidence is rapidly accumulating that this operation plays a logical and important role in the management of mitral stenosis. The historical aspects and technical details of valvulotomy are beyond the scope of this paper. The present indications and contraindications for operation may be seen in Table XII.

TABLE XII. INDICATIONS AND CONTRAINDICATIONS FOR MITRAL VALVULOTOMY

Indications.—
Tight mitral stenosis 1 sq. cm. or less as determined by any four of the following eight:
Severe exertional dyspnea on one flight
Moderate or marked left auricular enlargement
Moderate or marked enlargement of the pulmonary artery
Right ventricular hypertrophy pattern in the electrocardiogram
Auricular fibrillation
Cardiac enlargement of 20 per cent or more
Hepatomegaly 4 cm. or more below the costal margin
3 to 4 plus edema
Contraindications.—
Evidence of active rheumatic fever
Subacute bacterial endocarditis
Major involvement of other valves
Mitral insufficiency

Refinements in case selection and surgical techniques have reduced the operative mortality so that it is now 1 to 5 per cent. Results are excellent in a high percentage of cases and improvement has been continuous.

Advances in cardiac surgery have begun to have their impact on various specialties including obstetrics. The clinician who steadfastly clings to the concept that maternal deaths from heart disease represent the natural evolution of rheumatic heart disease can scarcely object to a procedure which favorably alters this course, specifically valvulotomy, unless he seriously believes that longevity would be increased by further compromising the heart and subsequently subjecting it to repeated burdens of pregnancy and cardiac failure. In this instance mitral surgery might still be championed if only to effect a tighter stenosis.

Valulotomy Prior to and During Pregnancy-Recorded Experiences

Burwell and Ramsay[9] mention 15 patients who became pregnant and delivered without cardiac difficulty following mitral commissurotomy. Table XIII summarizes the reports of 35 patients operated upon during pregnancy. There were 2 deaths in these 35 patients; one due to irreversible pulmonary vascular changes (Burwell and Ramsay); the other not documented (Mason). Seven patients were still undelivered at the time of report (Parkinson, Tillman, Gorenberg, Watt and co-workers). One patient developed postoperative mitral insufficiency which necessitated therapeutic abortion (Burwell and Ramsay). The remaining 25 patients were benefited by operation and apparently completed pregnancy successfully and were delivered vaginally of normal viable infants although complete details regarding delivery and the baby were given in only 15 instances. Premature onset of labor occurred in only one patient (Cooley and Chapman) whose labor ensued 62 hours following valvulotomy at 36 weeks and this baby survived. Three patients developed emboli, one on the twelfth postoperative day (Watt and associates) and 2 in the postpartum period (Cooley and Chapman, Watt and associates). No other complications were noted. The time of valvulotomy was recorded in 23 instances: 12 in the first trimester, 4 in the second trimester, and 7 in the third trimester. The earliest operation was at 2 weeks and the latest at 36 weeks. Complete data including catheterization findings were included in only three reports. Pathologic examination of the auricular appendage was described in only two cases, both of which showed microscopic evidence of carditis (Parkinson, Tillman).

Valvulotomy at the New York Lying-In Hospital

Tables XIV and XV summarize the valvulotomy data from the Lying-In Hospital. One patient underwent commissurotomy two years prior to the pregnancy under consideration and five patients were subjected to operation during pregnancy. All patients had complete studies, including x-ray, electrocardiogram, vital capacity, blood count, sedimentation rate, c-reactive protein and antistreptolysin O titers, cardiac catheterization and biopsy of auricular appendage and lung. All showed evidence of cardiac failure prior to operation. X-ray revealed left auricular enlargement and pulmonary con-

TABLE XIII. MITRAL VALVULOTOMY DURING PREGNANCY

AUTHOR	CASE	AGE	PARITY	GRAVIDITY	WEEK OF OPERATION	CATHETERIZATION DATA	RESULT
Cooley and Chapman[10]	1	28	0	i	28	+	Term vaginal delivery. Mother, baby well
	2	23	0	i	36		Vaginal delivery 62 hours after operation. Mother, baby well
Logan and Turner[11]	3	27	0	i	16	+	Term vaginal delivery. Hemiplegia. Mother, baby well
	4	26	i	ii	12	+	Vaginal delivery. Mother, baby well
Brock[12]	5		0	i	12		Vaginal delivery. Mother, baby well
	6		i	ii	28		Vaginal delivery. Mother, baby well
	7		iii	v	28		Vaginal delivery. Mother, baby well
Parkinson[13]	8	25	0	i	9		Patient also tuberculous. Biopsy showed carditis. Undelivered at time of report
Baker, Brock, Campbell, and Wood[14]	9				12		Term vaginal delivery. Mother, baby well
	10				28		Term vaginal delivery. Mother, baby well
	11				28		Term vaginal delivery. Mother, baby well
Burwell and Ramsay[9]	12						Five patients did well. No details
	13						
	14						
	15						One patient died due to irreversible pulmonary vascular changes
	16						
	17						One patient developed serious mitral insufficiency and had therapeutic abortion
	18						
Mason[15]	19						Three patients did well. One died. No details given
	20						
	21						
	22						
Rumel[16]	23						No details given
Sommerville[17]	24				36		No details given
Tillman[18]	25	19	0	i	12		Biopsy showed carditis. Undelivered at time of report
Gorenberg[19]	26	25	0	i	12		Term vaginal delivery. Mother, baby well
	27	28	i	ii	2		Term vaginal delivery. Mother, baby well
	28	29	i	ii	12		Undelivered at time of report
Watt, Bigelow and Greenwood[20]	29	30	ii	iv	8		Term vaginal delivery. Mother, baby well in 3 cases. One had pulmonary embolus post partum. Recovered
	30	37	iii	iii	16		
	31	28	ii	ii	12		
	32	31	0	ii	16		
	33	26	0	iii	10		
	34	33	ii	iii	12		
	35	23	i	ii	20		Four patients still undelivered at time of report. All doing well. One had pulmonary embolus on tenth postoperative day

gestion in each instance. Electrocardiogram showed a right ventricular hypertrophy pattern in four cases (1, 3, 4, and 5). All six patients had normal P-R times. Catheterization studies showed all patients to have pulmonary

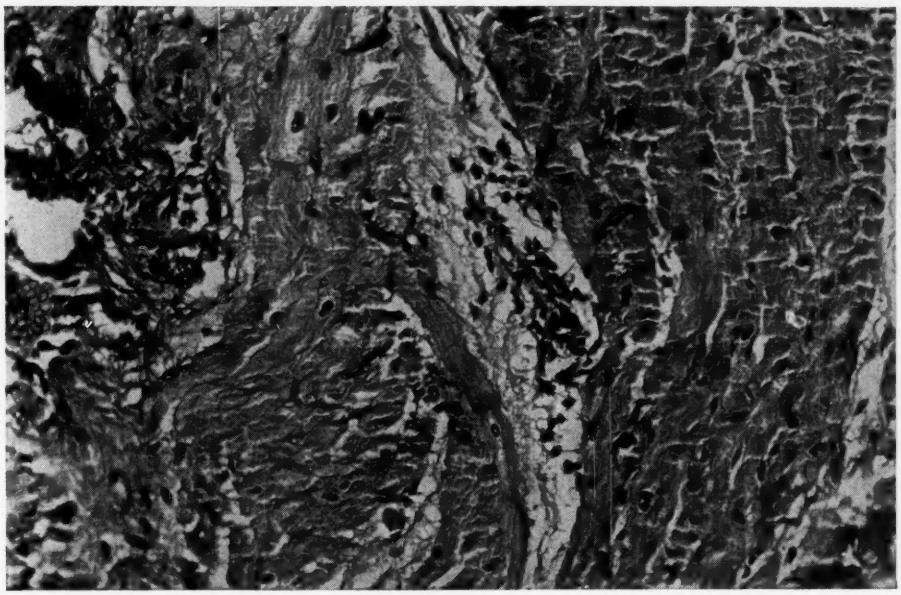

Fig. 1.—Section of the auricular appendage in Case 1 showing an Aschoff body in the myocardium.

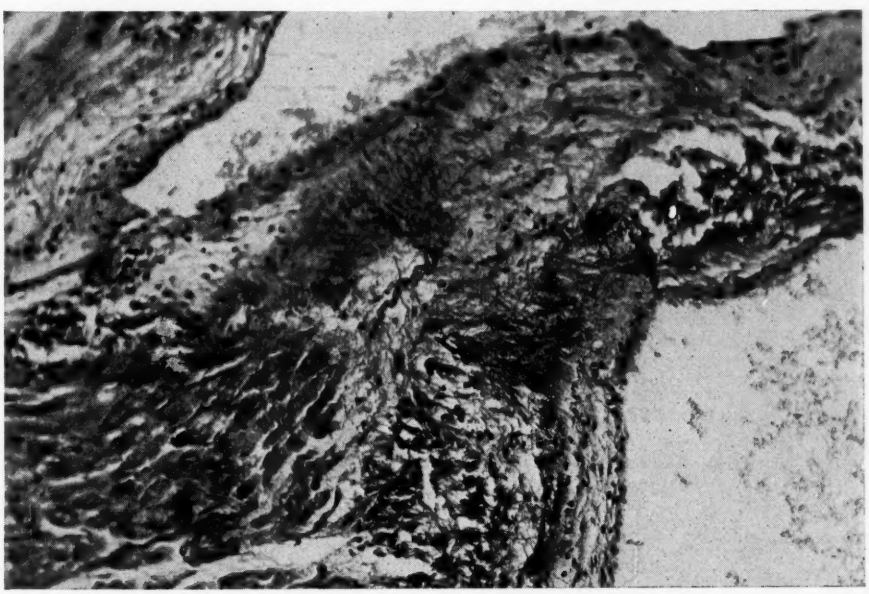

Fig. 2.—Section of the auricular appendage in Case 3 showing Aschoff bodies in the myocardium.

hypertension and tight mitral stenosis without insufficiency. Pathological examination revealed hypertrophy of the cardiac muscle in all cases, Aschoff bodies in two cases (1 and 3), pulmonary arteriolosclerosis in five cases

TABLE XIV. VALVULOTOMY AT THE LYING-IN HOSPITAL

CASE	AGE	PARITY	GRAVIDITY	X-RAY		ECG		ANTISTREPTOLYSIN O titer	C-REACTIVE PROTEIN	SEDIMENTATION RATE	W.B.C.	VITAL CAPACITY	WEEK FAILURE	WEEK OPERATION	VALVE SIZE 1 SQ. CM. OR LESS	PATHOLOGY			RESULT
				SIZE LEFT AURICLE	CONGESTION LUNGS	RHYTHM P-R TIME	RIGHT VENT. HYPERTROPHY									CARDITIS	ARTERIOLOSCL.	FIBROSIS LUNG	
1	35	i	ii	Enlarged	Cong.	N. S. R. 0.14	RVH	0	4 plus	35	3.5	2,150	18	19	+	+	+	+	Transient myelitis due to Efocaine paravertebral nerve block. Term vaginal delivery. Mother, baby well
2	40	iii	iv	Enlarged	Cong.	N. S. R. 0.16		0	0	35	14	2,700	16	18	+	0	+	+	Vaginal delivery at 35 weeks. Transient puerperal fibrillation and pulmonary embolus. Mother, baby well
3	24	0	i	Enlarged	Cong.	N. S. R. 0.16	RVH	0	2 plus	30	7.7	2,800	16	17	+	+	+	+	Transient fibrillation. Term vaginal delivery. Mother, baby well
4	32	i	ii	Enlarged	Cong.	N. S. R. 0.18	RVH	0	0	33	9.0	1,900	16	17	+	0	+	+	Transient fibrillation. Pulmonary edema at 27 weeks. Premature vaginal delivery at 28 weeks. Puerperal psychosis, mother well. Baby died (1,070 grams)
5	21	0	i	Enlarged	Cong.	N. S. R. 0.16	RVH	0	0	28	9.0	2,100	17	19	+	0	+	+	Term vaginal delivery. Mother, baby well
6	35	i	-	Enlarged	Cong.	N. S. R. 0.12		0	0	40	8.0	3,400			+	0	+		Valvulotomy two years prior to pregnancy. Multiple fibromyomas, miscarriage at 4 months
	37	i	ii	Enlarged	0	N. S. R. 0.12		0	0			2,400							Mother well, no evidence of decompensation

TABLE XV. CARDIAC CATHETERIZATION DATA

	REST							EXERCISE						
	NORMAL	CASE 1	CASE 2	CASE 3	CASE 4	CASE 5	CASE 6	NORMAL	CASE 1	CASE 2	CASE 3	CASE 4	CASE 5	CASE 6
Oxygen consumption in c.c./min./M^2	120-180	177	129	136	137	141		300 ± 50	391	391		224	225	
Arterial oxyhemoglobin saturation in %	96	90.8	93.4	93.2	95.5	96.7		96	100	90.8		97.2	96.7	
Arteriovenous oxygen difference in vol. %	4.0 ± 0.5	2.38	3.36	4.52	3.15	4.26		6.5 ± 0.5	6.0	8.63		6.03	6.30	
Cardiac output in L./min.		7.44	6.61	5.15	6.22	5.05			6.52	7.80		5.34	5.48	
Cardiac index in L./min./M^2	3.4 ± 0.4	5.47	3.84	3.01	4.32	3.30		4.4 ± 0.5	4.78	4.53		3.71	3.58	
Pressures in mm. Hg.														
"Pulmonary cap"	8-10	26	18	36	29	21	16	8-10	56	45		47	29	
Pulmonary artery	25/8	51/24	36/15	84/39	49/28	35/19	44/16	25/8	85/50	78/37	105/39	80/41	49/24	
Syst./Diast.														
Mean	15	33	25	60	35	28	22	15	68	56	73	58	35	
Right ventricle	25/2	51/8	42/3	85/10	47/3	35/4	47/5	25/2-4	71-10			76/8	51/3	
Right atrium	< 5	2	1	4	3	0		< 5	5	11	13	3	0	
Pulmonary vascular resistance in dynes/sec./cm.$^{-5}$	100	64	84	372	77	157		100	147	112		165	249	
Mitral valve area in sq. cm.	4-6	2.4	1.9	1.0	1.3	1.7			1.7			1.1	1.9	
Mitral insufficiency pattern	0	0	0	0	0	0	0	0	0	0		0	0	

(1, 2, 3, 4, and 5) and pulmonary fibrosis in 4 cases (1, 2, 3, and 5). The two patients with Aschoff bodies also showed elevated c-reactive protein levels but had no other clinical or laboratory evidence of active rheumatic fever (joint manifestations, fever, prolonged P-R time, leukocytosis, increased sedimentation rate, or elevated antistreptolysin O titer). Figs. 1 and 2 show sections of the heart revealing Aschoff bodies in Cases 1 and 3.

Comment on Catheterization Findings in Table XV

Case 1.—The most striking finding was that of the degree of pulmonary "capillary" hypertension at rest and during exercise. This pressure (a measure of the pressure in the pulmonary veins) was therefore in the range of the plasma protein osmotic pressure at rest and twice as high during exercise, creating the setting for pulmonary edema. The pulmonary arterial pressure was increased in proportion to the pulmonary venous pressure since there was no increase in the pulmonary vascular resistance as is common in a tight mitral stenosis. It was of great importance that the cardiac output at rest was considerably higher than normal; this might be ascribed to pregnancy and apprehension. It was also significant that although the output fell during exercise its actual level was normal for this degree of exercise (bicycling movement of legs while lying supine). The fall in output could be attributed to a lessening of apprehension during exercise.

The high pressures could be attributed to the increased output at rest. The pulmonary venous hypertension might be related to the hypervolemia of pregnancy. The mitral orifice was narrow enough to produce considerable difficulty in pulmonary hemodynamics when the patient was under stress. Accordingly mitral valvulotomy appeared to be indicated.

Case 2.—A moderate degree of pulmonary "capillary" and arterial hypertension was present at rest. During exercise, however, high-grade hypertension developed. The cardiac output was normal at rest but did not increase appropriately during exercise. The pulmonary vascular resistance was normal. The degree of stenosis was sufficient to produce considerable abnormality during exercise. It could be expected, therefore, that as the burden of pregnancy increased the difficulties might become progressive and pulmonary edema might develop. Mitral valvulotomy was indicated on these grounds.

Case 3.—The hemodynamics were characteristic of severe mitral stenosis with moderate sclerotic changes in the pulmonary vascular bed. The pulmonary venous ("capillary") pressure was very high at rest. Indeed, it was above the level of the plasma protein (25 to 30 mm. Hg) which is also the usual range for the resting pressure in tight mitral stenosis. The pulmonary arterial pressure was increased somewhat out of proportion to the pulmonary "capillary" pressure because of the increase in pulmonary vascular resistance. The resting cardiac output was within normal limits.

Since the pulmonary "capillary" pressure was so high at rest the usual five-minute leg exercise was shortened to two minutes in order to avoid the development of pulmonary edema. Both pulmonary venous and arterial pressures attained very high levels. Mitral valvulotomy was definitely indicated.

Case 4.—The hemodynamic pattern was of the type seen in tight mitral stenosis without associated pulmonary vascular disease. The cardiac output was high at rest probably largely due to anxiety although pregnancy may also have contributed. The fall in output during exercise may have been related to the fact that the grade of activity performed was less of a stimulus for an increase in output than anxiety. It is also possible that the right ventricle was not able to maintain the high pulmonary arterial pressure that was generated. The work of the right ventricle was greater during exercise. Because of the good right ventricular function and little change in the pulmonary vascular bed the patient was an ideal candidate for mitral valvulotomy.

Case 5.—This was the hemodynamic pattern of a moderately stenotic mitral valve without associated pulmonary vascular changes. The cardiac output was normal at rest

but increased only slightly with exercise. The pulmonary vascular pressures were moderately elevated. The hemodynamics were severely enough disturbed to warrant mitral valvulotomy.

Case 6.—Because of difficulty in obtaining arterial blood the procedure was prolonged and a complete study precluded. Pulmonary "capillary" and arterial pressures were obtained. There was definite hypertension in both the venous and arterial segments of the pulmonary circuit. The increase in pulmonary arterial pressure was proportional to the elevation of pulmonary "capillary" pressure, which indicated that the pulmonary arteriolar resistance was probably normal.

Repeat catheterization was refused on all occasions.

Satisfactory finger fracture of the mitral valve was obtained in all instances without production of mitral insufficiency. A markedly constricted mitral valve measuring 1 sq. cm. or less was encountered in each patient. Valvular calcification occurred in only one patient (Case 4) and here only to a minor degree.

Case 6 successfully underwent valvulotomy two years prior to pregnancy and was subsequently placed in the Class 2 functional group. Her pregnancy was complicated by multiple fibromyomas and a spontaneous miscarriage occurred in the fourth month of pregnancy. She remained in Class 2 and her course was otherwise uncomplicated.

Antepartum operations were performed between the fourth and fifth months. All patients survived operation and pregnancy. Case 4 developed attacks of pulmonary edema associated with panic reactions at the height of the circulatory burden. The other 4 patients showed progressive improvement without cardiac insufficiency.

Case 1 developed a transient myelitis due to Efocaine paravertebral nerve block performed to prevent postoperative chest pain. She has since shown almost complete recovery and is in no way incapacitated. Additional instances of central nervous system complications following use of this agent have been reported[21] and its use has since been discontinued. Three patients (Cases 2, 3, and 4) developed transient auricular fibrillation postoperatively for the first time. Case 2 had a small pulmonary embolus post partum. Case 4 developed a transient postpartum toxic psychosis not associated with rheumatic activity (the c-reactive protein was normal and the auricular appendage negative for Aschoff bodies).

Case 4 had a 7 month premature spontaneous vaginal delivery three months post valvulotomy. The baby, a normal immature infant that weighed 1,070 grams, died within 24 hours. The remaining 4 patients delivered normal viable infants per vaginam, 3 at term and one at 35 weeks. All 4 infants survived.

Comment

A careful study of the Class 3 and Class 4 group will aid in selection of patients who should be considered for therapeutic abortion and/or valvulotomy. The importance of thorough and complete investigation cannot be overemphasized. We recently saw a patient with mitral stenosis and repeated bouts of hemoptysis. Catheterization data revealed an adequate mitral valve with satisfactory hemodynamics and tomograms subsequently disclosed a hitherto unrecognized bronchiectasis. Without complete studies this patient might well have been considered a suitable candidate for valvulotomy. Catheterization studies have similarly given us reason to advise against valvulotomy in four other obscure cases. Catheterization is well tolerated during pregnancy.

Occasionally in severe mitral stenosis valvulotomy is either technically impossible because of advanced pathological changes, or contraindicated because of concomitant high-grade mitral insufficiency or aortic valve involvement. Here one must rely on supportive measures or vaginal therapeutic abortion. Subsequent refinements in cardiac surgery may have something to offer these patients in the future. If gestation has advanced to the stage where vaginal abortion is no longer technically feasible, experience has shown that the hazards of abdominal intervention may be as great or greater than allowing the pregnancy to continue with supportive measures alone. Here practically all authors are in agreement. One occasionally encounters a borderline situation in early pregnancy where hysterotomy can be performed before the predictable cardiac burden has become manifest, but in general abdominal interruption is definitely contraindicated.

Should preliminary therapeutic abortion be performed (where feasible and acceptable) if commissurotomy is contemplated? The heart's ability to withstand gestatory burdens can best be appraised if the results of valvulotomy are fully determined prior to conception but the theoretical disadvantages of mitral surgery during pregnancy may be doubted on careful consideration.

First, pregnancy may increase the risk of commissurotomy. There are two recorded deaths in forty cases. This 5 per cent mortality rate is no higher than that associated with operation in the nonpregnant state. Furthermore, this figure compares favorably with the 20 per cent mortality rate accompanying cardiac failure during pregnancy.

Second, cardiac surgery may increase fetal mortality. Premature labor could possibly be related to surgery in only one instance (Cooley and Chapman) and this baby survived. Another patient became worse after operation and required therapeutic abortion. Neither antepartum death of the fetus in utero nor fetal abnormality occurred. Fetal salvage was undoubtedly increased in patients who survived operation and these results outweigh the fetal loss from 2 maternal deaths and one therapeutic abortion.

Third, the mitral valve may be found inoperable at time of surgery or significant mitral insufficiency may be produced, either condition leaving the patient unchanged or worse. Proper selection of candidates, including careful x-ray study, will reduce the incidence of inoperability due to advanced calcification. Women in the childbearing age are less likely to have such changes than men of the same age or older women. One of our patients (Case 4) had calcific deposits but only in mild form which did not interfere with valvuloplasty. Furthermore, such operative failures would be immediately apparent and interruption could still in almost all instances be performed postoperatively. This procedure was carried out in Burwell and Ramsay's case.

Fourth, pulmonary vascular changes may occasionally be irreversible. Only one instance has been reported (Burwell and Ramsay). Here again careful selection of candidates with complete catheterization study will reduce the likelihood of this rare complication.

Fifth, a postoperative flare-up of active carditis may occur. Pathologic examination of auricular appendages secured at valvulotomy has raised the question of latent clinically unrecognizable rheumatic activity. In some series Aschoff bodies have been found in as high as 45 per cent of cases. In the nonpregnant patient postoperative carditis has not been consistently correlated with positive biopsy. Aschoff bodies have occurred in patients without fever, pericarditis, joint symptoms, chorea, leukocytosis, elevated sedimentation rate, elevated antistreptolysin O titer, or prolonged P-R time. In our 2 cases with positive biopsy, elevated c-reactive protein titer afforded the only positive correlation. However, Aschoff bodies and elevated c-reactive protein in the absence of other clinical or laboratory evidence of rheumatic activity have not adversely influenced results of successful valvuloplasty where hemodynamics had been altered by mitral obstruction. British authors[22, 23, 24, 25] have stressed the importance of carditis as a major factor in mortality from rheumatic heart disease during pregnancy. Their conclusions now seem to have been based on postmortem histological evidence similar to the incidental positive biopsies being obtained from auricular appendages. Documentation of their fatal cases did not include a description of the mitral valve so that mechanical obstruction cannot be discounted as the cause of failure and death.

We have suspected carditis in only 10 pregnant rheumatic cardiac patients and this diagnosis was definitely established in 4. Clinical or laboratory evidence of rheumatic activity was absent in all 21 cases of chorea, all 21 cases of chronic auricular fibrillation, and all fatal cases of rheumatic heart disease. None of the 8 autopsied patients showed Aschoff bodies. There were no deaths in 17 patients with first-degree heart block. We shall continue to look for active rheumatic fever, especially where failure cannot be correlated with the degree of predictable hemodynamic burden or severity of mitral stenosis, but we seriously doubt that active carditis plays a significant role in our cases of rheumatic heart disease or that it has contributed to our maternal mortality. In fact, the rarity of clinical carditis during pregnancy suggests that the gestatory state may exert some protective influence, possibly in the form of elaboration of adrenal hormone.

Sixth, although improvement begins soon after successful valvulotomy, it may be slowly progressive even for years, and the hemodynamic burden of pregnancy may be at hand before adequate benefits materialize. Our Case 4 is the only recorded instance to date that would substantiate this hazard and the patient survived.

Seventh, commissurotomy benefits may be temporary because of valvular refusion. This is most unusual and has not complicated any of the recorded cases complicated by pregnancy.

Eighth, auricular fibrillation seen in severe mitral stenosis would constitute a contraindication to pregnancy. It is found for the most part in advanced rheumatic heart disease and will therefore occur in a relatively high percentage of patients considered for valvulotomy. To date this has not been a significant problem preoperatively, although it has come up as a transient

complication in 3 of our cases following operation. Whereas auricular fibrillation and carditis are frequently associated in younger patients, this relationship is not seen in women of the childbearing age as previously indicated. The arrythmia creates greater risks of decompensation and embolism but we have learned that the management of pregnancy complicated by chronic auricular fibrillation should not differ from that of pregnancy complicated by equally severe rheumatic heart disease with normal sinus rhythm. Successful commissurotomy will decrease the likelihood of cardiac failure, thrombi may be removed and the judicious use of anticoagulant drugs will further lessen the incidence of embolic complications. Experience has indicated that cardiac catheterization should be omitted where there is a previous history of embolism.

One may gather from the foregoing paragraphs that the hazards of valvulotomy during pregnancy are more apparent than real. We embarked on this study, performing valvulotomy and allowing pregnancy to continue. To date we have not had occasion to regret this decision which was designed to obtain a live mother and a live baby. Future experience may lead us to alter this approach.

At what stage of pregnancy should commissurotomy be performed? The earlier operation is undertaken the sooner will benefits accrue before the circulatory burden asserts itself and the more opportunity there will be to resort to interruption in the event of surgical failure. Experience has shown that operation can be performed almost any time, even during the period of greatest hemodynamic strain. If this stage has already passed it would appear advisable to defer surgery until after pregnancy. Cooley and Chapman admit the dubious wisdom of performing their valvulotomy at 36 weeks but assert that the sooner operation is done the earlier will the patient be able to assume added responsibilities of the new baby. The onset of labor could possibly be related to operation in only one instance (this same case of Cooley and Chapman).

We have not altered our concepts of antepartum, intrapartum, or postpartum management of patients with rheumatic heart disease[26] following valvulotomy. Vaginal delivery with appropriate shortening of the second stage of labor is employed barring other obstetric indications for cesarean section. The incidence of spontaneous abortion and premature labor, the weight of the baby, the duration of labor and the blood loss at delivery in women with serious rheumatic heart disease are not significantly different from values in normal women. However, the advent of mitral valvulotomy and the future prospects of intracardiac surgery should materially reduce cardiac indications for therapeutic abortion and sterilization. The latter need no longer be considered an accessory to interruption of pregnancy.

One cannot but marvel at current advances in medicine and surgery. Their impact on our specialty is inevitable. Ten years ago how many would have questioned the sanity of an obstetrician who advocated finger fracture of the mitral valve during pregnancy. Perhaps we shall see the day when valvular pathology can be prevented by therapeutic agents. How obsolete this paper will then appear.

Summary

There have been 78,527 pregnancies at the New York Lying-In Hospital from Sept. 1, 1932, through Dec. 31, 1953. Heart disease was diagnosed in 2,932 patients (3.7 per cent). There were 29 deaths in these 2,932 patients, a mortality rate of 1 per cent. Cardiac disease is responsible for 23 per cent of all deaths at this institution. Ninety per cent of the heart disease is of rheumatic etiology and approximately 75 per cent of patients have mitral stenosis. The deaths from heart disease occurred for the most part in a relatively small group of patients with severe mitral stenosis. Decompensation and death are related to the predictable and unpredictable hemodynamic burdens of pregnancy. The management of severe mitral stenosis is considered with respect to supportive therapy, therapeutic abortion, and mitral valvulotomy.

The literature concerning mitral commissurotomy and pregnancy is reviewed and experiences at the Lying-In Hospital recorded. Sixteen patients (including one from this institution) undertook pregnancy subsequent to valvulotomy and all went through pregnancy without cardiac difficulty. One patient had multiple fibromyomas and miscarried at the fourth month. There was no other recorded fetal mortality. Forty patients (including 5 from this institution) underwent valvulotomy at varying times ante partum from the second to the thirty-sixth week of gestation. All but two survived; one of these had irreversible pulmonary vascular changes, the other case is not documented. Abortion had to be performed in another patient following operation because of severe mitral insufficiency. The remaining 37 patients did well.

The onset of labor could possibly be related to operation in only one instance and this baby survived. Another patient delivered prematurely three months following operation. There was no other recorded fetal mortality.

The various theoretical disadvantages of performing commissurotomy during pregnancy are questioned.

The importance of careful individualization and thorough study, including cardiac catheterization, is stressed and the ramifications of valvulotomy, including active rheumatic fever, auricular fibrillation, and sterilization, are discussed.

Conclusions

Cardiac disease is today the single greatest cause of maternal death at the New York Lying-In Hospital. Severe mitral stenosis is largely responsible for this mortality.

The onset of cardiac decompensation and the time of death can be definitely related to the predictable hemodynamic burden of pregnancy. It is this burden rather than the natural course of rheumatic heart disease which accounts for the vast majority of maternal deaths, all statistics pertaining to age at death in rheumatic males and females notwithstanding. Childbearing does not shorten life expectancy in rheumatic heart disease *provided* the patient survives the hemodynamic burden of pregnancy.

Cardiac catheterization is well tolerated during pregnancy. In selected cases it offers a direct and accurate method of appraising the extent of mitral stenosis and cardiac reserve.

Every case of mitral stenosis during pregnancy must be carefully individualized. Supportive therapy, therapeutic abortion, and mitral valvulotomy each play a definite role in our present concept of the problem. None is a panacea.

The obstetric ideal of obtaining a living mother and a living baby is most logically approached by improving the ability of the heart to withstand the burdens of pregnancy.

The ability of the heart to withstand gestatory burdens can be best evaluated if the benefits of valvulotomy are fully determined prior to pregnancy.

Mitral valvulotomy can be successfully performed ante partum. Pregnancy does not increase the operative mortality of mitral commissurotomy. The danger of premature labor following valvulotomy is not significant.

Valvulotomy during pregnancy requires special consideration in terms of inoperability, mitral insufficiency, irreversible pulmonary vascular changes, carditis, progress of hemodynamic improvement, valvular refusion, and auricular fibrillation. These hazards are at present more apparent than real.

The recorded experiences indicate that mitral commissurotomy prior to and during pregnancy favorably influences maternal and fetal mortality.

Clinically recognizable carditis is an extremely rare complication of pregnancy and has not occurred in our cases of severe mitral stenosis.

Obscure rheumatic activity as suggested solely by elevated c-reactive protein level and presence of Aschoff bodies in the auricular appendage has not interfered with the success of valvulotomy where the hemodynamics had been altered by mitral stenosis.

Carditis, clinical or latent, has not been a factor in our maternal mortality.

Women in the childbearing age with mitral stenosis are not likely to have valvular calcification which would interfere with the success of commissurotomy.

Accepted concepts of antepartum, intrapartum, and postpartum management of patients with mitral stenosis are not altered by valvulotomy except that indications for therapeutic abortion and sterilization are decreased.

Sterilization need no longer be considered an accessory to interruption of pregnancy.

Cardiac surgery has made childbearing possible for women heretofore doomed to barren marriage by severe mitral stenosis.

All patients from the Lying-In Hospital were critically reviewed preoperatively by the cardiovascular team consisting of representatives from the various clinical departments of the New York Hospital—Department of Surgery: Dr. Frank Glenn, Dr. Ward O'Sullivan; Department of Medicine: Dr. Harold Stewart; Department of Anesthesia: Dr. Joseph Artusio; Department of Pediatrics: Dr. Mary Allen Engle; Department of Radiology: Dr. Israel Steinberg; Cardio-Pulmonary Laboratory: Dr. Dan Lukas;

valvulotomies were performed by Dr. Frank Glenn with the assistance of Dr. Ward O'Sullivan. Dr. R. Gordon Douglas, chief of the Department of Obstetrics and Gynecology, gave considerable time and aid to this investigation.

This study was made possible by the combined efforts of these colleagues, and I wish to express my appreciation for their various contributions.

Addendum.—Since this article was submitted for publication, we have performed six additional mitral valvulotomies during pregnancy without serious incident. All six patients delivered normal viable infants. Another patient subjected to mitral valvulotomy prior to pregnancy also delivered a normal viable infant.

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Discussion

DR. ALVIN J. B. TILLMAN.—The availability of commissurotomy has furnished the obstetrician with a short cut in the management of the pregnant cardiac patient with mitral stenosis. The brilliant results reported tonight will prompt many attempts throughout the country to duplicate or excel them. I have therefore taken it upon myself in the role of discusser to sound a note of caution.

The purpose of commissurotomy during pregnancy is the relief of pulmonary hypertension. As a result, the dangers of heart failure removed, and maternal and fetal salvage are accomplished. Indirectly a great economic saving to both the patient and the community may occur since when the evidence of congestive failure disappears, prolonged hospitalization, standard practice in the management of this case, appears no longer necessary. This is a great comfort to the patient and her family.

In mitral stenosis, narrowing of the valve beyond a critical point obstructs the flow from the pulmonary capillaries and pulmonary veins so that if blood flow to the ventricle is to occur and cardiac output is to be maintained, the pressure must be increased. With the passage of time the pulmonary and left auricular pressure increase, and the cardiac output decreases. In normal pregnancy, however, it has been frequently demonstrated, most recently by Hamilton, that the cardiac output rises from the tenth week sharply,

and at the twenty-sixth to twenty-ninth (5.7 L. per minute) is 25 per cent more than in the nonpregnant period (4.5 L. per minute). In addition, there is increase of blood volume with the plasma volume out of proportion, and the velocity of blood flow is increased. These factors predispose to heart failure. It is still unsettled whether these values return to normal levels in the last three to four weeks of pregnancy.

Reports obtained from the nonpregnant postoperative commissurotomy patients indicate a variability in (1) an increase in cardiac output, although actually little change has been reported (Dexter, Baker), (2) a fall in pulmonary capillary pressure, (3) a variable fall in pulmonary arteriolar resistance immediately, with a more pronounced fall occurring many months later. The lack of immediate response to the surgical procedure has been explained by another factor responsible for the hemodynamic changes in mitral stenosis, namely, pulmonary atherosclerosis. In long-standing mitral stenosis changes occur in the small arteriole which, when severe, increase resistance to blood flow and so result in pulmonary hypertension. In addition, vasoconstrictor mechanisms are said to be present and, in those cases where pulmonary arterial pressure falls immediately postoperatively, vasoconstriction is said to exist rather than arteriosclerosis.

Theoretically, then, in pregnancy many factors persist following commissurotomy which tend to induce failure in the damaged heart. These are particularly evident after the twelfth week of gestation. Furthermore, resulting from both pregnancy and mitral stenosis, they do not tend to clear for a long time after operation. Improvement which has been seen to occur during pregnancy must take place because the pulmonary capillary pressure and vasoconstriction were the most important factors operative at that time. The risk remains that unless the case is most carefully selected, the results will not be good.

The mortality rate of pregnant cardiac patients today is very low in competent obstetrical hospitals. Some have said that pregnancy does not cause death from heart disease when strict supervision is maintained throughout pregnancy. With this I cannot agree, but I do agree that the death rate from heart disease can be kept extremely low, under 1 per cent, when therapeutic abortion is judiciously employed. This death rate under conventional therapy must be kept in mind when commissurotomy is contemplated. The best reports speak of a 5 per cent death rate, and this is relatively recently in the hands of surgeons who have had much experience in this field. Bland in 1952, reporting 352 cases taken from the reports of surgeons, gave a mortality of 15 per cent and the listed improvement of the patients varied from 58 per cent to 87 per cent. Maloney and Blalock, in a report two months ago, said that if embolism could be prevented, the mortality should be under 5 per cent. The pregnant cardiac patient has a well-recognized propensity for emboli.

All authorities agree that rheumatic fever is a contraindication to surgery in the mitral valve. Fortunately in this instance active carditis is relatively uncommon in pregnancy but it is of some interest to note that 25 to 45 per cent of biopsies on auricular appendages acquired at commissurotomy have shown Aschoff bodies. There is one report available which describes a syndrome occurring several weeks after operation in 43 of 179 consecutive cases of commissurotomy which the author considers reactivation of rheumatic fever. Of the 43 patients, 3 died, 4 became psychotic, 2 developed hemiplegia, 5 developed permanent auricular fibrillation.

In the very few cases of commissurotomy during pregnancy with which I am familiar, premature delivery occurred only once. This occurred in the case reported by Cooley two days following surgery, the case to which Dr. Mendelson referred. Premature labor should be expected in this procedure in at least the incidence seen in any major surgical procedure.

The criteria for selection of a suitable case for commissurotomy are in constant flux today. In the nonpregnant there are those who want to operate on mitral stenosis regardless of disability and point to the high mortality in complicated cases. The study of Bland and Jones is a propos. These writers reported on 1,000 cases followed for 20 years, since childhood or first attack of rheumatic fever. Pure mitral stenosis was found in only 117

cases and only 12 had signs of serious pulmonary hypertension. They pointed out that even the pure form of mitral stenosis need not always represent a high degree of narrow orifice; also that slight lesions accompanied by little or no cardiac enlargement may be well borne for years without serious disability of progression.

The more conservative approach in the selection of suitable candidates insists upon a tight mitral stenosis with some symptoms of pulmonary hypertension such as dyspnea, cough, orthopnea, pulmonary edema, and hemoptysis, a minimal degree of insufficiency, auricular fibrillation. Contraindications, in addition to active rheumatic fever and bacterial endocarditis, are marked mitral insufficiency or an aortic lesion with all cardiac chambers enlarged.

It seems to me that the most important criterion for selection during pregnancy depends upon whether the procedure may save life. This requires experience and judgment. While many patients with mitral stenosis undergo pregnancy with little, if any, disability, there are a few with a very tight stenosis who as a result of the load of pregnancy promptly go into heart failure. Many give a history of failure in a previous pregnancy, in labor or shortly afterward, and recover promptly only to have failure earlier in a subsequent pregnancy. These are treacherous cases and the prognosis must always be guarded. It is this type of patient who, if other criteria are fulfilled, becomes a suitable subject. We have one such patient now on the wards, but she has refused surgery. She was so well in the nonpregnant interval that the surgeons refused to operate on her at that time.

The brilliant results reported most conservatively by Dr. Mendelson tonight tend to nullify a great deal of what has been pointed out in the discussion, but even in Dr. Mendelson's collected cases in which patients have delivered and data are complete, comprising 26 patients, there was an incidence of 2 deaths, 8.8 per cent mortality, a failure in one case, 3.9 per cent, and a hemiplegia, 3.9 per cent, in another patient.

When the procedure is successful, there can be little question that a great deal has been accomplished, the symptoms of failure are relieved, and the dangers of cardiac death are lessened. Nevertheless, in our present knowledge, commissurotomy must be used cautiously until surgical mortality approaches the mortality from pregnancy.

DR. HAROLD E. B. PARDEE.—I have a great respect for the beneficial effects of commissurotomy in the cases of mitral stenosis. It will be most desirable if we can find the women who intend to be pregnant and who are going to be in trouble during pregnancy and have them operated on beforehand.

The problem arises when we see a woman during pregnancy who is in danger of developing severe heart failure. Commissurotomy is an operation of considerable severity and has a mortality rate in the neighborhood of 5 per cent in women who are not pregnant. Pregnancy possibly increases this mortality. There follows a period of convalescence of perhaps three months during which pain may be a very disturbing feature. There is also the possibility of the postoperative development of persistent auricular fibrillation, which condition itself adds gravity to the prognosis for labor.

For patients who refuse to have the pregnancy interrupted, however, and who are in a serious way because of the state of their hearts, management by surgery is apparently successful in many cases. Patients who do not refuse interruption I believe are better off even in the second trimester to have this done and then to have the valvulotomy and try again to become pregnant.

I do not think that the operation should be performed after the fifth month. The postoperative reaction is sometimes severe and lasts for a month or six weeks. Some patients develop a postoperative rheumatic exacerbation. Dr. Mendelson has not had that experience but it happens occasionally and affords an unpleasant though usually not dangerous complication. I think I have made it plain that I see a place for this procedure but that I would not recommend it unless the patient will not allow interruption.

DR. HAROLD GORENBERG.—I disagree with much that Dr. Mendelson has said. I disagree with so much that I can answer in the time allotted only a few of the criticisms he presented.

He talks about the predictable burden of pregnancy and depicts it in the form of a curve. There is no doubt that pregnancy is a burden. The curve that was shown is the curve of the rise and fall that occurs in the blood volume during pregnancy in the patient with and the patient without cardiac disease. The predictable buden to a great extent is a function of the rise and fall in the blood volume during pregnancy. A very good piece of work on the rise in blood volume has recently been done by Dr. Hillary Hamilton in Great Britain. Her figures are just a little bit less than those which we previously accepted. It has been believed that the rise in cardiac output was between 25 and 50 per cent at the height of the pregnancy. Her data, which are based on a larger number of patients, give figures a bit lower—between 17 and 25 per cent as the rise in cardiac output during pregnancy. Although there are other factors to be considered, it may be said that the burden on the heart is something in the neighborhood of 17 to 25 per cent over normal at the height of pregnancy.

Now we also have figures on what the burden which is imposed by various activities in ordinary life is. For example, it has been estimated that very concentrated thinking by Dr. Einstein for a period of an hour on a complicated problem entailed an energy expenditure that could be satisfied by the eating of half a salted peanut. Simple physical activities, as sitting, standing, dressing, and undressing, have been shown to cause a rise in cardiac output of about 25 to 50 per cent. Light household duties have been shown to require an increase in cardiac output of 100 to 200 per cent over the resting state.

Our argument is that although a weakling might be overwhelmed or greatly fatigued by carrying a 50 pound weight, he could drop that 50 pound weight, take on a 25 pound weight, and have no distress. It is our belief, then, that if you take away the ordinary daily ambulant activity from a woman when she is pregnant, you will be taking the big weight away; the 50 pounds will be taken off her shoulders, and she will be able to carry the relatively slight predictable burden of pregnancy.

Our experience at the Margaret Hague Hospital has shown that we have some reason to believe this. We have now a series of almost 600 consecutive clinic cases. Dr. Mendelson quoted the word "consecutive" from our article but he left out the next word "clinic," i.e., "consecutive clinic" cases. It has been explained to Dr. Mendelson a number of times why we separate our "clinic" cases from our "private" cases, and when it was explained he seemed to understand that there was good reason for doing so.

This is in part not an unusual way of dividing cases. Dr. Fitzgerald of Chicago has recently reported on 450 of his clinic patients. He reports 3 deaths. Those 3 deaths occurred, by the way, in patients who had therapeutic abortions performed. He had no deaths in patients who did not have any operative interference. At the same time he states that in 200 nonregistered cases at the same hospital the death rate from rheumatic heart disease is 9.4 per cent. He justifiably does not include those in his clinic group, because they did not receive the benefit, as undoubtedly there is a benefit, which his clinic offers.

We are dividing our cases for the same reason. At the Margaret Hague Hospital we have an open staff. There are somewhere between 200 and 300 doctors delivering patients at the Margaret Hague on private services. We don't state that the management they give is good or bad. We only say that their management is not the management we have set up in our clinic and therefore we should not include those cases in our results. In our almost 600 consecutive clinic patients who were managed according to a certain system of rules we had 2 deaths. Both deaths occurred in patients in whom the rules had been violated for reasons that I do not have time now to go into.

Our rules are: (1) Every pregnant woman with heart disease should go to bed for an hour or two every afternoon. (2) The patient who is 25 years of age or older should be seen in the clinic every week. (3) A patient who has Class 3 or 4 heart disease before pregnancy is to be hospitalized an soon as she registers at the clinic and kept at absolute bed rest until delivery. (4) The patient who has a history of cardiac failure in the past should be hospitalized at her first visit to the clinic and kept at absolute bed rest until

delivery. (5) The slightest decrease in cardiac reserve should be searched for at each clinic visit, and recognized; and the patient should be hospitalized if there is the slightest indication that her reserve is decreasing. (6) Cesarean section is not to be done on the indication of heart disease.

We know that cardiac failure is the problem. We say that our job then is to prevent decompensation, not treat it; the six rules just given do prevent heart failure.

Dr. Mendelson has said that he is convinced that longevity is not adversely influenced by pregnancy if the patient survives the pregnancy. Our follow-up studies have shown that that is true. And it is true in spite of the hazards of succeeding pregnancies. We maintain that our rules do allow the cardiac patient to survive the pregnancy.

Pregnancy is a peculiar right of a woman and it cannot be compared to something like appendicitis. We have shown that the application of certain rules during pregnancy can prevent death in the cardiac patient, and follow-up studies show her life expectancy is not shortened. Therefore, we believe it is fair to state that abortion has no place in this problem.

If a patient is seen early enough for abortion, then she has been seen early enough for good management, good medical care, and she may be allowed to go through a successful pregnancy.

Dr. Mendelson has stated that valvulotomy has decreased the need for abortion. We believe that this operation is a significant advance in the treatment of certain cardiac patients pregnant or nonpregnant, and have employed it with excellent results in 3 pregnancies. The fact remains, however, that our rules of management have decreased the need for abortion to the vanishing point.

DR. MENDELSON (Closing).—I am grateful to the various discussers for their remarks. I fully agree with Dr. Tillman and his words of caution regarding indiscriminate valvulotomy. I have stressed the necessity of complete investigation including preliminary cardiac catheterization.

We have attempted to obtain a live mother and live baby and therefore have performed commissurotomy without interruption of pregnancy. Although the total experience is still limited, the results to date justify this approach. Unless further data alter these findings I cannot agree with Dr. Pardee that the life of the baby should be sacrificed.

It is true that Dr. Gorenberg has previously explained his "consecutive" series to me, but I have never seen the logic in his method of analysis. Whereas the statistics he quotes are a credit to his personal management of the pregnant cardiac patient, his regimen of absolute bed rest has not solved the total problem of cardiac maternal mortality at the Margaret Hague Maternity Center or at the New York Lying-In Hospital. Hypervolemia of pregnancy in severe mitral stenosis cannot be consistently compensated for by the reduction in cardiac output incident to bed rest, and for the same reason decompensation and death cannot be consistently prevented. If failure could be prevented there would by definition be no Class 4 patients.

Lack of time must have prevented Dr. Gorenberg from discussing the three patients he has subjected to valvulotomy during pregnancy. Perhaps he too believes this procedure plays a role in management of the problem. My remarks were not intended to provoke controversy but to shed light on a condition which ranks as the number one killer of pregnant women.

THE PRESENT STATUS OF HUMAN MALE INFERTILITY*

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THE relative position of male infertility in the over-all problem of human infertility remains a matter of considerable debate. During the past 10 years, however, several sound studies on semen quality in apparently normal men and in cases of infertile marriage have tended to define more rigidly our assessment of the infertile male. I believe it is appropriate to review these studies briefly at this time to determine, primarily, if there is reasonable agreement among authorities.

The Significance of the Sperm Count

In any discussion of male infertility perhaps the greatest emphasis is placed on the sperm count. In this regard, the statement of Meaker[18] that in his experience "no pregnancy has occurred in cases where the sperm count was below 60,000,000" has had more influence upon students and practitioners in the field of male infertility than any other single pronouncement in the literature. Meaker's statement was universally interpreted as meaning 60 million cells per cubic centimeter and while he did not actually add the term "c.c." there is little doubt that he intended to do so. As a result and for many years, 60 million sperm/c.c. has been considered as the lowest count consonant with normal male fertility, and treatment of the infertile male has been based upon this premise. In perspective, it is difficult to understand how Dr. Meaker's conclusion, based on sparse evidence, could have been taken in such literal fashion. Since 1934, abundant evidence, based on reliable analyses, shows clearly that normal conception and pregnancies are produced with sperm counts far below the 60 million/c.c. level. Hotchkiss and associates[10] in a series of 200 fertile men found 25 per cent with counts below this "magic" figure, and we, in a study of 1,000 men of proved fertility, found a similar number (29 per cent) in the same range. Many other similar investigations on smaller groups of men (e.g., Falk and Kaufman[7] on 100 men) reach essentially the same conclusions. There is no doubt at all that a more realistic appraisal of male fertility in terms of sperm count must be made. A most important consideration is whether a line of demarcation can be drawn above or below which a man can be considered fertile or infertile or whether there is a rising potential of fertility with increase in sperm concentration. If sperm concentration were the only factor in the potential fertility of any given semen specimen, these points could be decided with relative ease. But we have no good reason to believe that a spermatozoon can produce conception unless it possesses motile activity. It is obvious, therefore, that men with true necrospermia, rare as they may be, are just as sterile as with aspermia, even though hundreds of millions of spermatozoa are present. Two further questions are inherent in any discussion of motile activity. The first is whether a

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few motile spermatozoa among millions of inactive cells are enough to ensure conception and, second, whether the *quality* of motile activity (i.e., the rate of forward progression) is not of fundamental importance. Most authorities would agree, I think, that a semen specimen in which 80 per cent of the cells are active is more fertile than one in which only 10 per cent of the cells show some degree of activity. But there is considerably less agreement and, unfortunately, even less discussion as to whether the cells must have a certain *quality* of activity before conception can reasonably be expected. One of the great difficulties is the lack of a common standard for estimation of quality of motility. It is rather easy to estimate the percentage of active cells and to transmit one's findings to another observer but the estimate of speed of progression of spermatozoa is a more subjective process and, as such, liable to varied interpretation. In spite of this handicap, most experienced observers in the field agree rather closely on what constitutes good, indifferent, or poor motile activity.

If we consider only sperm count and motile activity as factors in male fertility and try to formulate standards on the basis of present evidence, there is general agreement that the 60 million/c.c. figure as the lower level of normal fertility is much too high. Williams,[24] in an estimate of "approximate tolerance to spermatic pathology," suggests a level of 40 million/c.c. with impaired fertility between 3 and 40 million/c.c. The experience and sagacity of Dr. Williams in the field of human sterility are well known, and his opinion must be given considerable weight. Tyler,[21] on the other hand, on the basis of 113 pregnancies in a total group of 408 infertile couples, claims that "the possibilities decrease considerably as the sperm count deteriorates and that, if anything, the present (1951) standard of 60 million/c.c. is too low." Tyler bases this conclusion on the fact that none of the pregnancies occurred in the 1 to 20 million/c.c. group and only 15 (13 per cent) where the sperm counts were 60 million/c.c. or less. These figures are in decided contrast to the general experience. Hotchkiss and co-workers, in their semen examinations of men whose wives were pregnant at the time of the examination, found that 25 per cent of the men had counts below 60 million/c.c. MacLeod and Gold,[15] in an exactly similar study of 1,000 men, derived a figure of 29 per cent under 60 million/c.c., with 5 per cent under 20 million/c.c., and 17 per cent below 40 million/c.c. Harvey and Jackson,[9] in 324 cases of infertile (not sterile) marriage, report that in the husbands who had either produced a conception in the marriage prior or subsequent to the semen examination, 21 per cent of them had counts under 50 million/c.c. and 8 per cent counts under 25 million/c.c. It is probable that if in this study the count level had been set at 60 instead of 50 million/c.c., the fertile group percentage would be about the same as that reported by Hotchkiss and associates and MacLeod and Gold.

At first glance, it appears that in all studies involving a population of reasonable size, by far the greatest number of conceptions are produced where the sperm counts are above 50 or 60 million/c.c. But these figures are most misleading inasmuch as they may be as they are simply because the sperm counts of most men are above the latter levels whether they be in a fertile or an infertile marriage group. The figures do *not* mean necessarily that *only* because the counts were above a 50 or 60 million/c.c. level did conceptions occur. For example, Tyler, in 113 conceptions did not find *any* produced by a sperm count under 20 million/c.c., a finding which is contrary to much reliable evidence in the recent literature. In our most recent study[17] of conceptions eventually produced in infertile marriage, 10 per cent of them occurred with sperm counts under 20 million/c.c., and we exclude aspermia from these figures. Tyler does not say if he included aspermia (43, or 10 per cent of the total number of couples studied) in the group under 20 million/c.c. Generally speaking,

Tyler's paper is deficient in certain information, e.g., how long his cases were followed up, and the data therein are not strictly comparable with those compiled by us.

Similarly, the data of Harvey and Jackson at first glance seem to indicate that by far the greater number of conceptions were produced by sperm counts above 50 million/c.c. But if, as they point out, the proportion of conceptions in relation to the number of men represented at each count level is examined, 40 per cent of the 5 to 25 million/c.c. group eventually produced conception, 50 per cent of the 25 to 50 million/c.c. group did likewise, as compared to 57 per cent in the 50 million/c.c. level. In fact, almost 10 per cent of the total number of conceptions in their study occurred with sperm counts under 25 million/c.c., and 21 per cent of them with counts under 50 million/c.c.

Last, Bender[2] in a most interesting analysis of 700 infertile marriages, in which, after 17 years' follow-up, 324 conceptions eventually took place, reveals that of 57 men with repeated counts below 10 million/c.c., 19, or 33 per cent, were apparently successful in impregnating their wives. Bender's conception rate (46.3 per cent) is remarkably high, but his follow-up period also was remarkably long. It is of interest to note that 20 per cent of the total conceptions occurred in men with counts under 40 million/c.c.

The data we have accumulated in a study of what now approximates 3,000 fertile and infertile marriages not only lead us to agree with Harvey and Jackson and with Bender but to do so with a degree of mathematical precision.

We believe that it is essential to study intensively what can be expected of large populations in order to interpret properly the eventual results in infertile marriage. If, as we have done,[15] the semen counts of two large populations are examined (1,000 men of known fertility and 1,000 men in infertile marriage) and the relative frequency distribution in terms of count per cubic centimeter of the two populations studied, the inescapable fact is that the only essential difference between the two groups lies at the 1 to 20 million/c.c. count level. Above that level, the curves of the frequency distributions of the two populations can be laid one on top of the other and make an excellent fit. If we go further,[15] taking only the infertile group of 1,000 men, and segregate those men who either had produced one conception in the marriage ("one-child sterility" is a common infertility classification) or a conception subsequent to a semen examination, and compare the frequency distributions of the counts in this population with those who never produced a conception, essentially the same state of affairs is found. There is a very significant difference between these two populations at the 20 million/c.c. or less level, but almost identical frequency distribution above that level. We have interpreted these facts to mean that, taking only sperm counts as the factor in male fertility, above the 20 million/c.c. level there is no gain in potential fertility. Recent evidence[6] gained by a study of successful conceptions in a series of 500 sterile marriages supports our conclusion. In lower mammals (rabbits and cattle) recent and, to us, most suggestive, work lends considerable credence to the idea that the sperm count per se is not the most important factor in male fertility. Willett[22] and his group at Wisconsin, in determining the minimal number of spermatozoa necessary to produce conception by artificial insemination in cattle, reach the provocative conclusion that above a level of 12 million/c.c. (total count in a volume of 1 c.c.) there is no increase in their conception rates. Below that count level, their per cent conception rates fell slowly but steadily until the million level was reached at which point the rate fell off sharply. While it is not strictly proper to compare conception rates produced by artificial insemination with those attained by coitus, we, nevertheless, submit that there is food for thought in the insemination figures.

More recently, Braden,[3] in a study of the distribution of spermatozoa in the genital tract of the female rabbit after coitus, states that "above a certain level, increase in the number of sperms deposited in the vagina at coitus apparently has no effect on the total number of sperms entering the Fallopian tubes." His findings are in agreement with those of Austin[1] who inseminated rabbits with known numbers of spermatozoa and with those of Chang,[4] who found that in the rabbit it made little difference in the number of spermatozoa eventually reaching the Fallopian tubes if 20 million or 10 million cells were inseminated. Thus, the conclusions reached in the rabbit by several different workers are essentially the same (virtually sperm for sperm) as those reached by Willett and his group in cattle. They conclude that the cervix and the uterotubal junction are most effective barriers against the passage to the tubes of the spermatozoa.

Therefore, the figure we have suggested for the lower level of normal fertility in the human being (20 million/c.c.) does not, in the light of the evidence cited, seem fantastic, particularly when, in these circumstances, a considerably larger total number of spermatozoa are deposited at or near the external os. If we consider an average ejaculate volume of 3 c.c. in man, the total number deposited would, at this low count per cubic centimeter level, be 60 million cells.

The Significance of Motile Activity

In the light of present knowledge we take it as axiomatic that unless a spermatozoon possesses motile activity, it cannot reach and fertilize the ovum. We shall assume, furthermore, and contrary to the opinion held by Moench,[19] that a sperm lacking motile activity in the ejaculate is not likely to attain motile activity in the female reproductive tract. Thus, it is not enough to say that a certain sperm count is present. We must also denote the percentage of active cells and ignore, for the moment, the quality of motile activity which these cells must possess. Farris[8] has suggested the number of motile spermatozoa as an index of fertility in man. In a study on 239 individuals, he showed that "no man with a total active sperm count of less than 83 million had been able to have children." He concluded that "it appears probable that men possessing less than 80 million active spermatozoa in the total ejaculate are subfertile." But Farris' own percentage active figures for the most fertile men in his series is only 46 per cent, which means that if we accept his 80 million active cells as a lower level of normal fertility, such individuals would have to possess at least a total of 170 million cells in the ejaculate, a figure not differing substantially from that already given by most authorities.

Falk and Kaufman,[7] in their study of 100 fertile marriages, report an average of 61 per cent active cells in the semen specimens of the husbands as compared to 58 per cent in the 710 fertile cases reviewed by MacLeod. There is rather unanimous agreement in the literature that a finding of 100 per cent active cells is exceedingly rare, that 80 per cent active is an excellent figure, and that 60 per cent active is a reasonable expectation in most cases where the period of continence preceding the specimen examined is not unduly lengthy.[13] Williams[24] allows a normal tolerance of 30 per cent inactive forms, a figure we believe on the high side. In our analysis of large populations[14] we found that impaired fertility is most often found when the percentage of active cells drops below 40 per cent, and it is at this level that a sharp difference between fertile and infertile population is found.

Furthermore, we have found there is a curious lack of emphasis in the literature upon the quality of motility or the speed and type of forward progression of the spermatozoa. Almost invariably "motility" is expressed as

"% motility" though what that expression means, apart from denoting per cent of active cells, it is difficult to determine. We already have commented on the lack of a good method of expressing quality of motility. Farris[8] proposed the hemocytometer method, a slight modification of a method suggested earlier by Harvey and Jackson,[9] by which the speed of movement of the cells across the accurately spaced lines of the chamber could be designated as millimeters progressed in seconds. In this manner, comparable results could be obtained by all observers and a "common language" of motile activity set up. We have used such a method at various times ourselves but never have found it to have a good correlation with the more subjective and, in our hands, at least, the more representative method of estimating the quality of movement of cells between slide and coverglass. We take the view that any experienced observer of semen quality can quickly tell the difference between good, poor, or indifferent motile activity and that he can transmit his impressions to others with relative ease.

For this reason, we shall discuss at this time only our own impressions of the relationship of quality of motile activity to the over-all question of male fertility.

In comparing the two large fertile and infertile populations,[13] a strong relationship between motile activity and fertility is found. There is a rising potential of fertility with increasing quality of motility, irrespective of the sperm count. At any level of quality, the fertile population has a better "per cent active" cells than the infertile group, and, conversely, for any given "per cent active," the fertile group has better quality. In this particular analysis, it was not possible to determine whether the "per cent active" cells or the quality of motility was the most significant. But when we studied the fertile group alone,[17] using as an arbitrary criterion the time taken to produce conception, we found that "quality of motility" was of much greater significance than sperm count, per cent active cells, or morphology. The median time taken to produce conception in this group was about 2 to 6 months, except when the sperm count of the husband was under 20 million/c.c., when the per cent of active cells was below 40, or when the quality of motility was poor. But the largest median time by far was found (8 months) when the quality of motile activity was poor. At the moment, our position is that the motile activity of the spermatozoa is of more significance than the sperm count and that, indeed, this quality of semen may compensate for other seminal deficiencies.

Morphology

The role of sperm morphology in human fertility has been a controversial question, particularly since Williams and Savage[23] found a high correlation between the breeding record of bulls and the morphology of their spermatozoa. Moench[19] adapted these techniques to the study of human semen and, using a most elaborate subdivision of the spermatozoa into various morphologic types, came to the conclusion that when the number of "abnormal" forms is above 25 per cent, sterility is inevitable. This troubled subject has been reviewed so many times by prominent workers in the field (Cary, Williams, Moench, Hotchkiss, Harvey and Jackson, Weisman, etc.) that further discussion here would be pointless. Not all of the workers in the field agree on what constitutes an "abnormal" form, although most have decided that, irrespective of other qualities of the semen, the presence of 20 per cent or more abnormal forms constitutes impaired fertility.

On the basis of our criteria of "abnormality," we cannot agree with such rigidity.[14] There is no doubt at all that, in comparing fertile and infertile

populations, sperm morphology at all sperm count levels is better in the fertile population. Furthermore, we find a rising potential of fertility with increasing "goodness" of morphology. These findings suggest that morphology *is* of considerable importance. But there also is a significant relationship between morphology and motile activity, and since there is a rise in fertility potential with increasing quality of motile activity, there remains the distant possibility that infertility, so far as sperm morphology is concerned, may be due more to the relatively poor motility shown by cells with abnormal morphology. When we correlate abnormal morphology with ease of conception, however, we fail to find the same high degree of significance as that found in the quality of motility. It is most unusual to find a high degree of abnormal morphology in the presence of an adequate sperm count and good motile activity. Rather is the converse true, namely, that the lower the sperm count, the more we are likely to find other defects in semen quality.[12] When highly abnormal morphology is present when the semen quality otherwise is good, and when there has been difficulty in producing conception with an apparently fertile female partner, then abnormal sperm morphology may be the causative factor in the sterility. Similarly, no positive evidence has ever been presented which links abnormal sperm morphology with accidents of pregnancy. We feel that the relationship of abnormal sperm morphology to the over-all problem of human infertility is unresolved but that the examination of morphology is an integral and essential part of every investigation of semen quality.

Continence and Semen Quality

In advising patients on sterility problems, the timing of intercourse is one of the major questions considered. It is essential for the gynecologist to know that the "fertile period" is covered adequately by the patients, and the urologist (or any specialist performing the semen examination) should be aware of the period of continence which precedes the procuring of the particular semen specimen submitted. Furthermore, we believe that in the treatment of sterility it is common practice to suggest that several days' continence prior to the expected ovulation time is valuable in ensuring that the semen quality be at its best. The latter approach appears to be based on the premise that the higher the sperm count, the better are the chances of conception and that a high sperm count can be attained by extending the intervals between coitus. These views and their validity are open to question in the light of recent knowledge.

What are the effects of continence on semen quality? The answer seems to lie in the semen quality of the individual under study. There does not seem to be any doubt that if the individual has a high sperm count (80 million/c.c. plus) after 3 days of continence, his sperm count is likely to be at least doubled after 10 days of continence.[16] But if cases of persistent oligospermia are studied after varying periods of continence, one finds it rather hard to predict what will result in terms of sperm count. The count may rise or fall, and if it rises when, for example, the period of continence is extended from 3 days to 10 days, the increase in sperm count is not appreciable after 6 days.[16] What is just as important is that, with increasing length of continence, the per cent of active cells decreases, so that what is gained in sperm count may be lost, in part, at least, by the increasing number of inert cells. One must ask if anything at all is gained by prescribing continence in sterility problems. If, as we have attempted to show, there is no gain in potential fertility with rising counts above a certain level and the individual has a good count after only 2 or 3 days of continence, why prescribe a longer period? His potential fertility will not be improved.

In the case of the individual with oligospermia, there is a degree of justification for extending the period between emissions in the hope of raising the sperm count, but what is gained in the count may be lost in motile activity. Of more significance, perhaps, is the rather provocative fact that in fertile marriage frequency of intercourse plays an important role in ease of conception; the higher the frequency, the better the chances of conception.[17] Whether this fact holds true in sterile marriage remains to be seen, but advising a *higher* rather than a lower frequency of intercourse in infertile marriage does seem to be a reasonable approach. Generally speaking, undue regulation of marital behavior in infertility may impose further strain in a husband-wife relationship which already is under severe emotional strain. The recent emphasis on psychosomatic factors in human infertility should be treated with respect. We believe that the practice of advising continence prior to a calculated ovulation time and a high frequency of intercourse during the so-called ovulation period does not serve any useful purpose so far as potential male fertility is concerned and may, indeed, negate the desired end. This is true particularly when the wife, by means of the temperature chart, is left to decide when ovulation is about to occur. The philosophy of "this is the night," or even worse, that "this is the hour," is conducive to emotional tension and therefore may actually inhibit ovulation when it does not inhibit the husband. If we make the reasonable assumption that the fertilizable life of the spermatozoon in the female reproductive tract is at least 12 hours (much reliable evidence would allow us to stretch this period considerably), a frequency of intercourse of 3 times weekly would maintain viable spermatozoa in the female reproductive tract throughout a major portion of the cycle. This would certainly be true of the husband with good semen quality. In oligospermia, where a few motile spermatozoa are found in the semen and where continence is not likely to improve the sperm count appreciably, it would seem more rational to maintain a regular frequency of intercourse and thus a few viable spermatozoa in the female reproductive tract at all times, than to disturb the couple by undue regulation of their marital life. No technique available at present allows us to pin-point the time of ovulation. Until that happy day arrives, we feel that the advisory approach just suggested will maintain a greater degree of marital happiness in infertile marriage and eventually produce more conceptions.

Comment

In this discussion, the position has been taken that the range of normal male fertility is much wider than has been supposed and that the sperm count per se is not the most important factor. There is little doubt that the figure of 20 million cells/c.c. we have suggested as the lower level of male fertility consonant with a reasonable possibility of conception will be subject to debate and perhaps scorn. The concept that the potential of male fertility does not improve with rising counts above a certain level may also be treated with skepticism, but the rising tide of evidence derived from several mammalian species supports the hypothesis suggested by the statistical analysis of human case histories. The emergence of the motile activity of the spermatozoa as a dominating factor in human male fertility should not be surprising. This activity may be considered as compensating in the presence of a low sperm count in the same manner as Falk and Kaufman have postulated for sperm morphology.

The physiology of the passage of the male germ cells from the ejaculate to the Fallopian tubes under conditions of normal coitus has, for obvious reasons, only been speculated upon. Our factual knowledge of the process is exceedingly scanty. In artificial insemination, for example, there is no sound evidence that inseminating directly into the body of the uterus produces better results than intracervical insemination. In the rabbit, Chang[4] noted that the number of sperm in the tubes is essentially the same whether artificial insemination or natural mating is employed, and Braden[3] has confirmed this finding in the same species. (It is of interest to remember that the rabbit ejaculate is quite similar to that of man in volume, consistency, and cellular count.) All of these workers agree that, in rabbits, the uterotubal junction and the cervix are the most important barriers in limiting the passage of *excessive* numbers of spermatozoa to the site of fertilization.

If we consider the known facts of deposition of human spermatozoa in normal coitus, the physical nature of the ejaculate at the time of ejaculation and for at least several minutes thereafter poses several questions. When produced directly into a receptacle and examined immediately, the ejaculate is a coagulum in the meshes of which the spermatozoa are immobile. There is and should be debate as to whether the nonmotile state of the spermatozoa at this stage is physical in the sense that they are unable to move against the great viscosity of the coagulated seminal fluid or whether they lacked motile activity at the moment they were projected into mixture with the fluids of the seminal vesicles and prostate. The visual evidence is in favor of already motile cells being inactivated by the physical state of their new environment. When the coagulum is examined microscopically during the early stages of liquefaction, two distinct phases can be seen, one in which the spermatozoa are immobilized in the coagulum but perhaps show vigorous tail movement, and the other, a fluid or liquefied phase in which the spermatozoa, now free, show vigorous, progressive activity. A brief transition phase can also be seen in which the sperm, once free of the "mesh," immediately show progressive motion as if they had been able potentially to do so.

Another important aspect of semen quality at the time of ejaculation is that most of the spermatozoa are expelled in the first third of the ejaculate.[11] Since we are accustomed to thinking of the efficacy of the sperm count in terms of count per unit volume and not total count, the importance of this massing of the spermatozoa in a relatively small forward portion of the ejaculate may have significance when two points, one of which we have discussed previously, are remembered. The first, as we have tried to show, is that, because of the immobility of the cells at the time of ejaculation, they cannot pass into the cervical canal at the moment of ejaculation by virtue of their *own* activity and may not be able to do so for at least several minutes. The second point to be considered is the relationship of the glans penis to the external os at coitus, under normal anatomical conditions and at the moment of ejaculation. Dickinson,[5] the acknowledged authority on human sex anatomy, shows, in these circumstances, that the lips of the meatus must be in contact with the external os in such fashion that the ejaculate is forced against or, as

far as is possible, into the mucus of the cervix. Thus, with the massing of the spermatozoa in the first portion of the ejaculate, a high concentration of spermatozoa would be forced against the external os and perhaps into the cervical mucus. Only a very small portion of the total ejaculate could be transferred to the cervical canal in this manner, but whatever its volume the concentration of sperm per unit volume (cubic centimeter) and not the total sperm count would be the deciding factor in the number of cells reaching the cervical mucus. The total sperm count would become a determinant only if we assume that migration of spermatozoa takes place from the semen remaining in the vagina after withdrawal. Just how much dispersion of the semen takes place over the vaginal surfaces is problematical. In such circumstances it is doubtful if, as has been postulated, an actual pool of semen forms in the vicinity of the external os. If this "pooling" does take place, one could imagine that random motile activity would allow migration of the sperm into the cervical mucus until such time as the vaginal acidity overcame the buffering action of the seminal fluid and destroyed the motility of the spermatozoa. If one transfers to the human the evidence obtained from other mammalian species, however, one must assume that most of the spermatozoa deposited in the cranial portion of the vagina at coitus do not progress beyond that point.[3] Relatively few spermatozoa reach the upper portion of the female reproductive tract in most mammals studied. From the experimental point of view, similar evidence in the human being will be exceedingly difficult to obtain, but, in the light of any reasonable thinking on the subject, the feeling remains that the passage of the spermatozoa from the male to the female genital tract under physiological conditions is a rapid process and is (1) probably dependent on the concentration per unit volume of spermatozoa in the first portion of the ejaculate and (2) limited by the resistance of the cervical mucus.

Summary

1. The evidence pertaining to the significance of the sperm count in human male fertility is discussed. It is suggested (1) that the range of male fertility in terms of sperm count is much wider than supposed, and (2) that the potential of male fertility above a certain level of sperm count is not related to rising counts.

2. There is a much closer relationship between quality of sperm motility and fertility potential.

3. The theoretical aspects of transference of the spermatozoa from the male to the female reproductive tracts under physiological conditions are discussed.

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Discussion

DR. MELVIN R. COHEN.—I was intrigued by Dr. MacLeod's discussion of Chang's work relative to too many spermatozoa causing a blighted ovum through superfertilization. I have done some intrauterine inseminations on a small group of patients who are infertile because of very poor cervical secretions which prevent sperm survival and cause failure of sperm migration upward. An example is a patient in whom a Hyams conization was performed for endocervicitis. For such patients, semen is obtained in a sterile receptacle and by means of a tuberculin syringe attached to a fine plastic catheter approximately 0.05 c.c. of semen is deposited in the uterus. I have had some success in a selected group of patients. I would like to ask Dr. MacLeod for his opinion of the dosage of spermatozoa for such intrauterine inseminations.

DR. MacLEOD.—I am afraid it would be difficult to perform intrauterine insemination under sterile conditions. The seminal fluid is contaminated at the source. I cannot speak for gynecologists in this matter, but I have detected an air of caution among most so far as intrauterine insemination is concerned. And there is no sound evidence that the latter has any advantage over the intracervical approach.

I believe, however, that your question was put to ask whether intrauterine insemination might tend to lead to polyspermy. I cannot answer that question except perhaps to point out that, in the lower species (e.g., rabbit), the uterotubular junction is an effective barrier against the passage of spermatozoa into the tubes, and it may be equally effective in the human.

QUESTION.—What effect does gonadotrophic hormone have on sperm?

DR. MacLEOD.—We have not used gonadotrophin therapy at Cornell in many years because we believe it is useless. There are reports that with its use inhibition of spermatogenesis is just as likely as stimulation. I believe the final test of gonadotrophin therapy in male infertility will come when the human hormone is available.

QUESTION.—Dr. Davis, what is your routine test for ovulation?

DR. DAVIS.—We use the basal body temperature to indicate ovulation in women who have normal ovarian function. Endometrial biopsies are obtained in women who have irregular menstrual periods. Studies of the endometrium provide pertinent information other than the occurrence of ovulation. The changes in the cervical mucus will indicate the ovulatory phase and our routine investigation includes a bacteriologic study of the endocervix to rule out the presence of infection. The cytologic study of the vaginal secretions provides a rather sharp end point for ovulation. However, this diagnostic procedure necessitates daily vaginal smears and experienced personnel.

DR. ANDREW McNALLY.—I would like to ask Dr. MacLeod if he has had experience with the rebound phenomenon.

DR. MacLEOD.—We have tried to repeat Dr. Heckel's findings but so far without real success. I wish I could say otherwise. It is only fair to say that we may not have followed the patients long enough. Dr. Heckel points out that one may have to wait for many months for the "rebound" though I must confess I find it hard to understand the physiological process involved in this latent period.

I should add, too, that we have used only the oral testosterone approach and testosterone administered parenterally *may* have a different effect. But we get the depression of spermatogenesis with oral testosterone, and I see no reason why, in such instances, we do not get the "rebound."

DR. EDWARD ALLEN: Dr. MacLeod, would you say a word about the nutritional elements in sterility?

DR. MacLEOD.—There does not seem to be any question but that the male germinal epithelium is a remarkably labile tissue and that it can be severely affected by relatively minor changes in the total organism. As such, I am sure that good nutrition and sound general health are important factors in male fertility. When I spoke of these factors, I meant that any obvious deficiencies in nutrition should be corrected. But in looking over the literature and analyzing our own data, it is difficult to assign to faulty nutrition a major role in the over-all problem of human male infertility. Glass has long maintained that liver function and, in this connection, the B complex are important in human fertility, and large doses of B complex may work in certain cases. But, in general, my feeling is that vitamin therapy has not been successful.

QUESTION.—What are the procedures at Cornell for aspermic patients? Do you do testicular biopsies?

DR. MacLEOD.—I do not do testicular biopsies personally, but I think I can speak for the men at Cornell who do so. Hotchkiss is reluctant to order the biopsy except in extreme oligospermia or, in aspermia, where it may be a question of differentiating between bilateral occlusion of the vasa or a disturbance of the germinal epithelium. More recently, I believe, there has been a trend among others to perform the biopsy when the sperm count may be at levels between 20 and 40 million/c.c. From the purely academic point of view, I welcome any information obtained on the relationship between the state of the germinal epithelium and the quality of the ejaculate. What is a normal biopsy? Many biopsies from apparently normal testes as well as from infertile men must be examined before we can dogmatize as to what condition of the germinal epithelium connotes a "poor" biopsy. I exclude from this reasoning, of course, the flagrantly abnormal biopsy in which one either finds no germinal epithelium or one which is so grossly disorganized as to give a good reason for the failure of sperm to appear in the ejaculate. According to the criteria of Warren Nelson and of Heckel, however, the testicular biopsy must be performed before "rebound" therapy is instituted in order to select the type of patient who should be given the therapy. We have not followed these criteria mainly, I think, because of squeamishness in indiscriminate use of the biopsy. The patient should be warned in every case that the testicular biopsy is diagnostic and is not likely to be of any help from a therapeutic point of view (the one exception is in suggesting surgery for repair of occlusion).

The question was asked about the success of anastomosis. I believe it is far better today than, say, ten years ago. Some writers claim 80 per cent success—I am afraid that figure is high. On the other hand, the necessity for this operation seems to be disappearing fast. We can thank antibiotics.

DR. IRVING F. STEIN.—I would like to ask Dr. Davis how, in cases of amenorrhea, he distinguishes between the various ovarian lesions. He demonstrated the conventional

hysterosalpingography with which we are all familiar, for evaluation of the tubal factor. Whether one uses opaque media or gas for the tubal patency test is not as important, in my opinion, as the technique employed for the procedure.

In addition to the tubal factor which has been emphasized by Dr. Davis and others, the ovarian factor in my opinion is of equal or greater importance. Hormone tests for the ovarian factors are not entirely reliable but there are other means of determining the ovarian status besides the usual pelvic examination. The normal pelvic status may be demonstrated by means of gynecography. Pneumoperitoneum will outline the normal-sized uterus and ovaries and the opaque medium will demonstrate the normal uterine cavity, the lumina of the Fallopian tubes, and intraperitoneal spill. I have demonstrated hypoplasia of the uterus and ovaries in a case of amenorrhea which was referred to me for consideration of surgery on the ovaries. Our diagnostic method demonstrated that in this case surgery was contraindicated. Bilateral polycystic ovaries have been demonstrated by pneumoperitoneum in a patient with a one-year amenorrhea in whom surgery was definitely indicated. In a patient who had never menstruated and in whom on bimanual examination the findings were very indefinite, pneumoperitoneum demonstrated the presence of ovaries and a vestige of the uterus represented by a median bar. The absence of both uterus and ovaries was demonstrated in a patient who also had absence of the vagina. Finally, a normal uterus and ovaries were demonstrated by pneumoroentgenography in a patient who had a nine months' amenorrhea. The film was of special value in convincing the patient that she had normal organs capable of functioning physiologically, and that the amenorrhea was most likely psychogenic in origin. The patient was convinced and resumed normal menstrual function after this explanation.

This method is useful in proving the presence of pathologic lesions, demonstrating the empty pelvis in the absence of pelvic organs, and in demonstrating normal genitals in cases of doubt where otherwise an exploratory operation would be required.

DR. M. EDWARD DAVIS.—Culdoscopy is a useful method of studying the ovaries in women with abnormal ovarian function. The visualization of the ovaries offers the most accurate means of making a diagnosis of polycystic ovaries. Although this diagnostic procedure is not without risk it should be used more widely.

I read a recent report that pregnancy followed resection of polycystic ovaries, Stein-Leventhal syndrome, in 70 per cent of patients subjected to surgery. If surgical approach to the therapy of this condition offers such excellent results an accurate diagnosis of ovarian pathology is essential.

EARLY PRIMARY ABDOMINAL (PERITONEAL) PREGNANCY*

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THE ability of the fertilized human ovum to achieve *primary* nidation on any peritoneal surface has long been a matter of considerable conjecture and controversy. In general, such a biological event has heretofore been considered by many to be impossible, but in recent years several well-documented cases have led to a better understanding and a changed concept of this situation. The phenomenon is of triple interest because of (1) the fundamental biological principle involved, (2) its rarity, and (3) its relationship to the treacherous problem of advanced abdominal pregnancy.

The literature on all varieties of abdominal pregnancy is now quite voluminous. Greenhill[1] has stated (1952) that nearly six hundred cases of abdominal pregnancy after the twenty-eighth week have been reported. The case reports, reviews, abstracts, and bibliographies of Cornell and Lash,[2] Gardner and Middlebrook,[3] Lull,[4] Hellman and Simon,[5] Beacham and Beacham,[6] Elzey,[7] Broomes,[8] Cross, Lester, and McCain,[9] Jarrett,[10] and Barrett[11] are comprehensive.

A selective review of the literature confirms the fact that the exact site of implantation in any abdominal pregnancy is frequently difficult, if not impossible to ascertain. The extensive placental attachments usually seen in moderately advanced or well-advanced (at or near term) abdominal pregnancies are usually of no help in determining the original site of nidation. Most of these advanced cases group themselves into two categories. In the first category, and certainly constituting the majority of cases, the placental attachments usually involve some serosal aspects of the uterus and tubes, the ovaries, the adjacent peritoneal surfaces of the pelvic and abdominal walls, broad ligaments, and near-by structures such as rectum, sigmoid, etc.; in a second smaller category of cases, wherein the products of gestation are located higher in the abdomen, structures such as small bowel, stomach, omentum, mesenteries, diaphragm, liver, and spleen may be the site of the placental attachments, with no placental continuity or relationship whatsoever to the tubes, ovaries, or uterus.

In the first category, most authorities agree that the placental attachments represent the end result of (1) an initial nidation in the infundibular region of the tube, or (2) an initial tubal ectopic pregnancy with either partial tubal abortion or slow perforation having taken place, or (3) a previously traumatized uterus with resultant uteroperitoneal fistula. Under any of these three circumstances the placenta retains enough of its original attachments to provide an

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intact and continuous blood supply for oxygenation and nutrition to the extruded or partially extruded sac and embryo. Further proliferation of the chorionic villi then takes place at the point of rupture and eventually involves large adjacent areas of peritoneal tissue, thus permitting continued growth and development of the entire conceptus.

In the second smaller category, wherein the placental attachments are remote from the tubes, ovaries, and uterus, the mechanism must be one of three, namely, (1) by primary peritoneal implantation, or (2) by a process of placental migration involving placental proliferation and atrophy (somewhat implausible), or (3) by complete tubal abortion or perforation and reimplantation. This latter concept of "reimplantation" or "secondary implantation" of a fertilized ovum at some other site in the pelvis or abdominal cavity, following complete tubal abortion, after such an ovum has initially undergone a primary nidation in the tube, has been difficult for most authorities to accept, and understandably so. While the chief biological role of the chorionic cell is "invasion" in a controlled sort of way, it seems reasonable that, following a tubal abortion, the completely detached and aborted products of conception, delicate and highly differentiated structures that they are, would have to have an intact and continuous blood supply rather than merely be bathed in the sanguineous environment accompanying tubal rupture or abortion, before such an aborted ovum could reattach itself someplace else and take up life anew. Novak[12] has summarized this concept by stating: "In many of the older descriptions, it was stated that if the ovum is expelled through tubal abortion or perforation, it might occasionally retain its vitality and reimplant itself upon the peritoneum at one point or another, most often on the tube, broad ligament, or upon adherent portions of the intestine. As a matter of fact, such a mechanism for secondary abdominal implantation is incredible even on a priori grounds. Certainly, the embryo would succumb the moment its separation from the tubal wall is complete." Faulkner and Douglass[13] and Curtis[14] have expressed similar views. Substantiating this viewpoint is the fact that no abdominal pregnancy has yet been reported following surgical treatment of an ectopic pregnancy wherein the products of conception were not recovered at the time of laparotomy, and presumably were left to their fate in the abdomen.

In true primary abdominal pregnancies, the trophoblast implants itself on a peritoneal surface without having undergone nidation at any other site. Where actual fertilization takes place is relatively unimportant—presumably, it could be anywhere in the pelvic or abdominal cavities. Following implantation, the placenta then comes eventually to involve extensive areas of peritoneal surface to such an extent that the original nidation site comes to be obscured, and, at surgery, such an implantation would be indistinguishable from the more common abdominal implantation which usually involves the area of the tube, ovary, and adjacent structures. The ability of the growing and maturing placenta to invade peritoneal tissues, as seen in those abdominal pregnancies which achieve an advanced stage, seems to be one of the most logical and

reasonable spheres of evidence to substantiate the validity of the concept of primary peritoneal implantation, since this chorionic activity is the basic physiological process underlying nidation, regardless of the site.

Ovarian pregnancies are of no help in clarifying the question of the site of original nidation in abdominal pregnancies. Probably most such ovarian pregnancies result from fertilization of an ovum which has not quite escaped its follicle, being fertilized "in situ," so to speak; possibly, some ovarian pregnancies result from fertilization of an ovum free in the peritoneal cavity, with subsequent primary nidation on the germinal epithelium; in neither instance can such an ovarian ectopic gestation be considered truly a "peritoneal" implantation, though it may eventually achieve the aspects of an "abdominal pregnancy."

Reports of early cases (8 to 10 weeks or less) in the literature, which are generally accepted as representing primary peritoneal nidations at sites other than the peritoneal surfaces of the uterus and tubes, include those of Gallabin[15] (1896, generally credited with reporting the first case), Witthauer,[16] Czyzewicz,[17] Jacquin,[18] Poten,[19] Tomasi,[20] Walker,[21] Williams,[22] Koehler,[23] Lee,[24] and Richter.[25] Elzey[7] has recently (1948) reported an early case (about 10 weeks' developmental time), with excellent discussion and bibliography, presenting impressive evidence for the concept of primary peritoneal implantation; in his particular case, the implantation occurred in the lesser peritoneal cavity. He also briefly reviewed three other comparable cases, those of Greene,[26] Nagel,[27] and Longley,[28] in which the implantation sites were the lumbar gutter, spleen, and retroperitoneal space, respectively. More advanced abdominal pregnancies considered primary because of the lack of anatomical relationship of the placenta to the tubes and ovaries, or because of lack of relationship of any of the products of gestation to the pelvic structures and pelvic peritoneum have been reported (authors cited by Elzey). Jacques[29] has reported a case in which, by posterior colpotomy, he delivered a 9 cm. fetus from a gestational sac on the posterior aspect of the bladder peritoneum, four years following subtotal hysterectomy and bilateral salpingectomy and right oophorectomy.

Reports in the literature of very early pregnancies which represent primary peritoneal nidation on the broad ligament include those of Hirst and Knipe,[30] Bourgeois,[31] and Steptoe.[32] Implantations on the serosa of the Fallopian tube, and there have been only two cases reported to date, include one by Hammacher,[33] in 1910, and one by Maxwell, Eastman, and Smetana[34] in 1927. Reports of peritoneal nidations on the serosa of the uterus include the cases of Meyer,[35] Ray,[36] and Studdiford.[37] The anatomical location of nidation sites on the serosal surface of the uterus, tubes, or broad ligaments, since they are so close to the sites of the most frequent types of extrauterine gestation (tubal and ovarian), immediately make these implantations suspect as to their true origin and pathogenesis. The case reported by Studdiford,[37] in 1942, involving an early ruptured pregnancy on the posterior aspect of the uterus, from its relationship to the peritoneum and to the interstitial portion of the tube, would seem to have established beyond any reasonable doubt the concept

of primary peritoneal nidation. It has served more than any other report to convince those previously dubious of the validity of this concept. Novak,[38] expressing some doubt in the first edition of his textbook, has stated in his most recent edition: "Until recently, there has been much skepticism as to the possibility of the fertilized egg implanting itself directly on the pelvic peritoneum, outside the genital canal, but the case reported in 1942 by Studdiford seems to establish the possibility beyond question. Moreover, this author has accepted as probably authentic several other cases from the older literature, especially that reported by Hirst and Knipe in 1908." Eastman,[39] likewise, has given Studdiford's case similar recognition and credit.

Studdiford believes that should the ovum be expelled from the follicle, then become fertilized and develop over a period of eight to nine days[40, 41] without being captured by the fimbriated extremity of the tube,[42] it would be most likely that nidation would then take place in any tissue, regardless of its origin, with which the blastocyst might come in contact; such tissue (excepting germinal epithelium of the ovary) would be either parietal or visceral peritoneum, and such a pregnancy should be labeled a primary peritoneal pregnancy. Studdiford further proposes the following criteria upon which the proof of such a pregnancy must rest: "(1) that both tubes and ovaries are normal with no evidence of recent or remote injury, (2) the absence of any evidence of a uteroperitoneal fistula, and (3) the presence of a pregnancy related exclusively to the peritoneal surface, and young enough to eliminate the possibility of secondary implantation following a primary nidation in the tube."

If, then, one accepts the premise and thesis that primary peritoneal nidation is possible, and it seems to be now generally accepted, one must also accept the possibility that a fertilized ovum *could* implant itself on the serosal aspect of the tube purely as a matter of chance. In such a case, then, the criterion that a tube must appear normal with no evidence of recent or remote injury could be nonvalid, since, obviously, a nidation on the tubal serosa would alter the otherwise normal appearance of the tube. Hirst and Knipe,[30] in 1908, and Best,[43] in 1931, in describing the necessary criteria for primary abdominal pregnancy, take cognizance of this point when they mention that there must be present a normal condition of the tubes, ovaries, and broad ligaments, *except where the ovum is implanted* (italics ours).

Case History

Mrs. W. E. H. (Swedish Hospital No. 51-7886) was first seen in the office of one of the authors (G. A.) on June 13, 1951, complaining of mild vaginal bleeding and lower abdominal discomfort. The patient was 26 years of age, twice married, with a medical background of an obscure history of rheumatic fever at age 12, with no sequelae. Surgical history revealed that in 1941 there had been a laparotomy because of a skipped menstrual period and abdominal pain, with appendectomy and left oophorectomy being performed. Menses started at age 12, had been regular in 28 to 30 day cycles, duration 5 days, with an occasional skip of a month or two. The last menstrual period started May 30, 1951, and had been normal, as had been the prior period. The obstetrical history showed two previous normal term pregnancies in 1943 and 1947.

According to the history of the current illness, the patient's last menstrual period had started at the time she anticipated that it would, but had continued in an intermittent manner until the date of the initial consultation, which was fourteen days after the period started. On the second day of the period, she had experienced lower abdominal discomfort which was constant, in contrast to her usual pre- and comenstrual dysmenorrhea. She had felt nauseated on several occasions, but there had been no vomiting; she had noted chilly sensations, but had not taken her temperature. There had been no other symptoms.

Physical examination revealed a young woman of medium build, appearing well. The abdomen was soft and flaccid with very minimal tenderness to deep pressure in the left lower quadrant. On pelvic examination, the cervix was smooth, firm, and closed; the uterus was forward, firm, normal in size and freely movable. In the left adnexal region there was a minimal degree of thickening and the structures were slightly tender. The right adnexal region was negative. On speculum examination the cervix appeared natural, and there was a little bloody menstrual-like discharge from the external os. Rectal-vaginal examination confirmed a little tender thickening high on the left side. The impression gained was that the patient had a mild endometritis and a subsiding, mild salpingitis. She was placed on a regime of bed rest, mild sedation, bland diet, bowel hygiene, fluids, and an oral tablet of 0.5 Gm. of sulfadiazine and 100,000 units of penicillin, four times a day, for five days. She was advised to report any unusual pain, bleeding, or any change in her status.

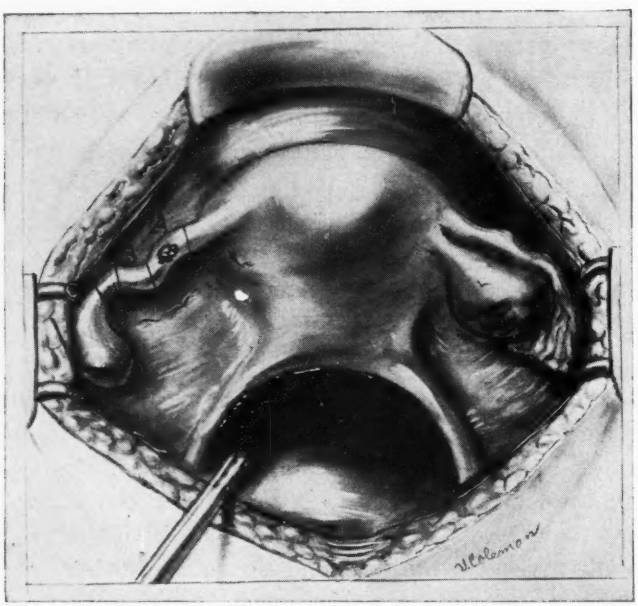

Fig. 1.—Operative view of the nidus *A* found on the peritoneal surface of the left Fallopian tube. Complete serial histologic sections cut at 3 microns were made through segments *A*, *B*, and *C*.

She followed this regime and reported on June 20, seven days after first being seen and 21 days after the onset of her last period, that she had been feeling better until that morning, when she then had a recurrence of mild pain but no other symptoms. Further rest was advised. In mid-afternoon of the same day, a relative reported that the patient had just experienced a sudden episode of severe pain in the lower abdomen, somewhat localized to the left side, followed by faintness, dizziness, and pallor. Immediate hospitalization by ambulance was advised, and, when seen within one-half hour after the onset of the pain, she was found to be in extreme agony and in early shock, with marked pallor, cool dry skin, pulse 96, blood pressure 90/50, temperature 97.2° F. The abdomen was rigid and extremely tender,

and on pelvic examination the vaginal fornices were boggy and exquisitely tender, and manipulation of the cervix caused the patient extreme pain. Rectal-vaginal examination yielded the impression of a boggy fullness in the cul-de-sac. In the meantime, intravenous fluids had been started, blood sent for, and laparotomy was scheduled. Preoperative blood count showed 3.9 million red blood cells and 16,750 white blood cells with a hemoglobin of 11.9 Gm. (76.5 per cent). The preoperative diagnosis was intra-abdominal hemorrhage, cause unknown, but possibly due to some variety of ectopic pregnancy. Under Pentothal sodium and cyclopropane anesthesia, the lower abdomen was opened through a midline incision. The pelvis and abdomen were found to be filled with fresh blood. The uterus was essentially

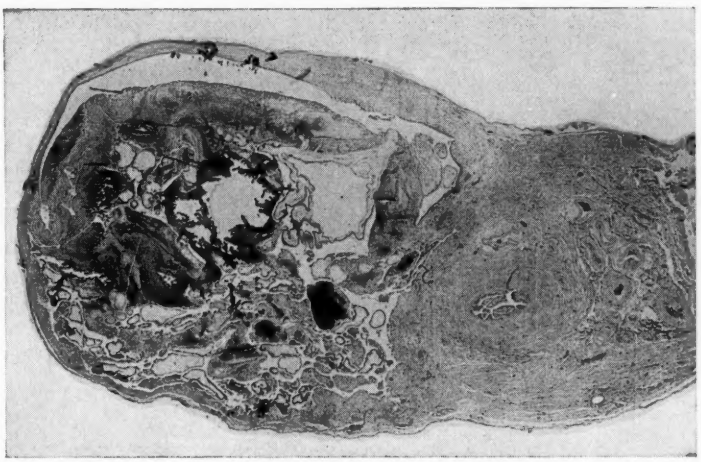

Fig. 2.—Photomicrograph of a section taken through segment *A* in Fig. 1, showing a cross section of the intact wall of the Fallopian tube with the pregnancy implanted on the peritoneal surface. (×9; reduced ¼.)

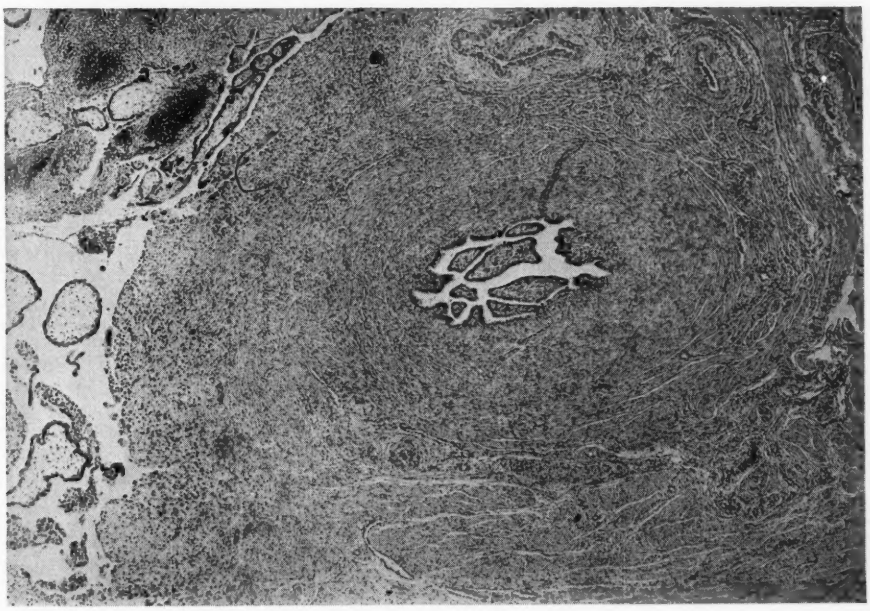

Fig. 3.—Higher magnification of Fig. 2 to demonstrate details of intact muscular and epithelial lining of Fallopian tube. The decidual reaction on peritoneal surface relating to chorionic villi is noted. (×45; reduced ¼.)

normal in size and color; the right tube was normal, as was the ovary, which also contained a recent corpus luteum. The left ovary was absent as a result of previous surgery. The left tube was tortuous and bulbous in its distal third, closed, smooth and blunted, with no evidence or suggestion of an ostium or fimbria at any point. On the superior-posterior aspect of the left tube, at a point about 1 cm. from the cornual insertion, there was seen a 1 cm. superficial hemorrhagic nodule which was bleeding most freely. There was no particular thickening, edema, or color change in the immediate adjacent portions of the tube and no evidence of gross rupture. Left salpingectomy was performed. Most of the blood was removed from the abdomen, and two units of blood were administered during and immediately following operation. Pulse and blood pressure stabilized during surgery, and her general condition improved gradually. The postoperative course was essentially nonmorbid and uneventful, with a single temperature rise to 100° F. on the third day. She received 300,000 units of penicillin daily for six days, and was out of bed on the second day, and ambulatory thereafter. On the fourth postoperative day, she was given a third transfusion of 500 c.c. because of a hemoglobin of 64.5 per cent. She was dismissed on the ninth postoperative day in excellent condition. She has felt well since. Follow-up pelvic examinations revealed nothing unusual. She has subsequently had two term pregnancies in another community.

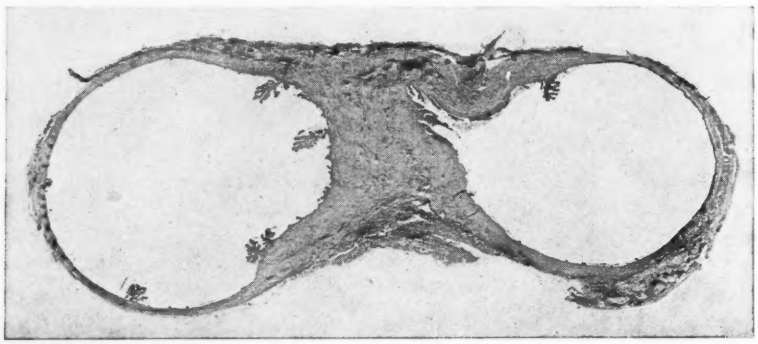

Fig. 4.—Representative serial section taken through bulbous and tortuous distal end of left Fallopian tube (segment *C* in Fig. 1) showing complete occlusion of lumen. The tortuosity of the tube is further evidenced by the double lumen. (×5; reduced ¼.)

Pathology

The gross picture of the left Fallopian tube with particular reference to the peritoneal nidus as viewed prior to surgical amputation is well illustrated in Fig. 1. The total length of the left tube measured approximately 8 cm. Appearing on the superior peritoneal surface 2 cm. from its cornual junction was an irregular, hemorrhagic, friable, and adherent nidus measuring 1 cm. in diameter. Prominent vascularity was noted surrounding the peritoneal attachment of the nidus and a small fresh blood clot was present on its outer surface. The remaining peritoneal surface of the left Fallopian tube was intact with no evidence of rupture or perforation. The distal end of the tube was sharply angulated, tortuous, rounded, and bulbous, with a complete absence of fimbria associated with a nonpatent lumen.

In order to carry out a comprehensive microscopic study of the nidation in relation to its peritoneal attachment, serial histological sections cut at 3 microns were made through the three segments of the left Fallopian tube (*A, B, C*) as indicated in Fig. 1. All sections through the tube showed the following: (1) an intact epithelial lining with no evidence of decidual or chorionic tissues; (2) an intact muscular wall with no evidence of a fistulous tract, perforation, or penetration relating to the nidus. These pertinent

anatomic findings make it evident that nidation in this case had taken place by primary implantation on the peritoneal surface of the left Fallopian tube (Fig. 2).

The method whereby nidation is possible beyond the confines of the endometrium is a matter of considerable interest. The ability of the peritoneum to respond by appropriate cell changes to a large variety of both pathologic as well as physiologic processes is typified by its ability to form decidua during pregnancy. This is well demonstrated in this case as noted in Figs. 2 and 3, where decidua has developed from the peritoneum corresponding to the site of nidation and extends into the subserosal area of the otherwise intact Fallopian tube. Serial sections failed to show any evidence that endometriosis formed the basis of either the decidual reaction or the site of nidation.

Further serial sections of the entire distal and bulbous end of the Fallopian tube substantiated the fact that there was complete occlusion of the lumen (Fig. 4). Taking into account this anatomic change, together with an absent left ovary (by previous surgical removal) and a grossly normal right ovary and right Fallopian tube, we believe that any other method of nidation than by primary peritoneal implantation is precluded.

Assuming a hypothetical mid-interval conception and deducting 7 to 9 days as having elapsed between fertilization and nidation, this pregnancy is estimated to be 25 to 27 days in development.

Conclusions

An early ruptured pregnancy (25 to 27 days) found on the serosal aspect of an occluded Fallopian tube has been described. Because of the unique clinical and anatomic circumstances present, and the confirming histopathologic findings, it is difficult to escape the conclusion that the blastocyst achieved this particular site by a process of primary peritoneal implantation. As far as can be ascertained, this is the third such case to be reported, wherein primary nidation has occurred on tubal peritoneum. We believe it adds further impressive evidence to substantiate the concept of primary peritoneal nidation.

We wish to thank Mr. Bernard Y. Flageolle for the preparation of the photomicrographic material.

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CARCINOMA OF THE BREAST IN THE PREGNANT AND THE NURSING PATIENT

Review of 1,375 Cases

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IN A previous article[151] it was pointed out that the combination of breast carcinoma and pregnancy, whether they occur simultaneously or the pregnancy follows treatment of the disease, is not necessarily hopeless. Ten cases of breast carcinoma were treated during pregnancy or lactation with 2 ten-year survivors, while 12 women became pregnant after treatment of breast carcinoma with 7 ten-year survivors. These 22 patients were drawn from a series of 1,304 carcinomas of the breast seen at the Bellevue, University, and Roosevelt Hospitals of New York City.

This material was then combined with a collection of 920 cases drawn from the literature between 1850 and 1950. The gross figures for survival from this analysis were 103 five-year survivors and 62 ten-year survivors of 734 patients treated initially for breast carcinoma during pregnancy or lactation. Of the 208 patients treated for carcinoma prior to pregnancy, 102 survived for five years and 35 for ten years.

The present article includes additional material reported through the year 1953. A total of 1,375 case reports have been collected from 144 published articles and numerous personal communications relative to carcinoma of the breast and pregnancy. All case reports are included, without selection, which could be found during a thorough perusal of the world literature in seven languages. Several hundred further articles made comments on this subject, but, since they did not contain new case material, they are not included in the present bibliography. The limited number in this series illustrates in part why there has been so much confusion and disagreement in regard to this problem.

Incidence of Carcinoma of the Breast and Pregnancy

A total of 43,931 cases of carcinoma of the breast reported by 29 authors includes 1,258 (2.9 per cent) patients in whom pregnancy or lactation was a complicating factor at some time during the course of disease (Table I). This is in agreement with the previous study[151] where 737 (2.9 per cent) of 25,159 cases of breast carcinoma had this complication. Furthermore, only 49 breast carcinomas were found on four large obstetrical services in a period when 161,624 pregnancies were seen (approximately 3 cases of breast carcinoma per 10,000 pregnancies) (Table II).

TABLE I. CASES OF PREGNANCY AND LACTATION FOUND IN SEVERAL SERIES OF PATIENTS WITH BREAST CARCINOMA

YEAR	AUTHORS	NO. OF CASES	COINCIDENT CARCINOMA AND PREGNANCY OR LACTATION	PREGNANCY OCCURRING AFTER TREATMENT	TOTAL CASES
1880	Billroth[13]	282	2	-	2
1882	Sprengel[135]	131	7	-	7
1900	Gebele[47]	340	1	-	1
1901	Polaillon[108]	226	3	2	5
1901	Rosenstein[120]	162	2	-	2
1912	Schwartzkopf[132]	395	7	-	7
1913	Saloman[124]	200	4	-	4
1921	Wiesmann[153]	106	2	-	2
1921	Wolff[156]	214	13	-	13
1924	Odermatt[99]	270	7	-	7
1929	Kilgore[76]	1,099	49	-	49
1930	Himmelmann and Lehmann[60]	268	7	-	7
1935	Höring[63]	195	1	-	1
1937	Meltzer[92, 139]	5,000	50	42	92
1939	Bromeis[16, 17]	2,000	42	14	56
1943	Haagensen and Stout[56]	876	29	7	36
1945	Putski and Scully[111]	205	1	-	1
1946	Kettunen[74]	656	16	1	17
1946	Westberg[150]	4,747	177	47	224
1946	Geschickter[48]	2,561	58	-	58
1949	Dargent, Mayer, and Archimbaud[30]	1,665	19	1	20
1949	Brooks and Proffitt[18]	395	6	5	11
1949	MacDonald[88]	5,213	42	-	42
1949	McLelland[91]	1,359	14	-	14
1952	Harrington[58, 59]	7,762	136	107	243
1952	Remold[116]	2,455	36	-	36
1952	Ahumada[4]	350	3	6	9
1953	Adair[2]	3,495	?	?	270*
1954	White[151]	1,304	12	10	22
Total		43,931	746	242	1,258 (2.9%)

*Incomplete information given as to when seen.

TABLE II. INCIDENCE OF BREAST CARCINOMA AMONG PREGNANT WOMEN

	PREGNANCIES	BREAST CARCINOMAS
Bellevue Hospital, New York City[151] January 1, 1933 to May 31, 1950	37,790	7
Geneva, Switzerland[78] 1907-1939	41,094	2
Elizabeth Steele Magee Hospital, Pittsburgh, Pennsylvania[109]	45,000	4
Presbyterian Hospital, New York City[56, 140]	37,740	36
Total	161,624	49

Age of Patients

The age was known in only 751 of the 1,375 cases included in this report. The average age of these patients was 35.8 years. The 584 who were pregnant or nursing at the time of treatment averaged 37.8 years, while the 158 who became pregnant after treatment averaged 34.8 years.

Delay in Treatment

Westberg[150] found that the pregnant or nursing woman reported a tumor of the breast an average of two months later than a parallel group of nonpregnant women. He also noted that the doctor delayed an average of one month

longer between first consultation and treatment in the pregnant or nursing woman with tumor than in the uncomplicated tumor. It was not possible to learn the patient delay factor in this series, but the doctor delayed an average of 3.1 months in the 521 patients in whom this delay was known. Both women and doctors often thought that the mass or other symptoms found were part of the normal sequence of events of pregnancy and were not concerned in many instances until the tumor became quite advanced.

An indication of the advanced stage at which many of these patients were seen is the large number of patients with inflammatory carcinoma, 52 of the 804 cases collected. A number of these patients had incision and drainage one or more times before the surgeon realized that he was dealing with a carcinoma. One of the patients in the previously reported series had incision and drainage without biopsy before it was realized that the patient had a breast carcinoma.

Results in Patients Treated for Carcinoma of the Breast During Pregnancy or Lactation

Of the 10 patients in the previously reported series, 6 were pregnant at the time of treatment and 4 were lactating. Two of the former group are alive after eleven years, while only one of the later survived five years. Including these, there were in the world literature 804 cases of pregnant or nursing women with carcinoma of the breast treated coincidentally. The gross five-year survival rate for the 484 patients reported since 1941 is 16.3 per cent (79 cases), with 11.8 per cent (57 cases) ten-year survivors. Of the 312 cases reported prior to 1941, 8.3 per cent (26 cases) survived five years and 3.2 per cent (10 cases) for ten years. The over-all improvement in reported results is quite marked.

TABLE III. SURVIVALS AMONG PATIENTS TREATED FOR CARCINOMA OF THE BREAST DURING PREGNANCY OR LACTATION

	WITHOUT METASTASES			WITH METASTASES			TOTAL		
		SURVIVALS			SURVIVALS			SURVIVALS	
	NO. OF CASES	5 YEARS	10 YEARS	NO. OF CASES	5 YEARS	10 YEARS	NO. OF CASES	5 YEARS	10 YEARS
Articles in literature, 1866-1940*	201†	21 (10.4%)	6 (3.0%)	64†	5 (7.8%)	4 (6.2%)	312†	26 (8.3%)	10 (3.2%)
Articles in literature, 1941-1953‡	195	59 (30.3%)	42 (21.5%)	289	20 (6.9%)	15 (5.2%)	484	79 (16.3%)	57 (11.8%)
White 1954	5	3	2	5	0	0	10	3	2
Total	401	83 (20.7%)	50 (12.5%)	358	25 (7.0%)	19 (5.6%)	806	108 (13.4%)	69 (8.6%)

*Refs. 3, 6, 9, 10, 12, 13, 14, 15, 16, 19, 22, 23, 24, 25, 29, 31, 32, 33, 34, 36, 37, 38, 39, 40, 42, 44, 47, 49, 50, 51, 53, 60, 61, 62, 64, 65, 71, 72, 73, 76, 79, 82, 83, 86, 89, 90, 92, 93, 95, 96, 99, 100, 101, 103, 105, 108, 112, 113, 114, 115, 117, 118, 119, 120, 121, 123, 127, 128, 129, 130, 131, 132, 134, 135, 136, 138, 139, 144, 145, 146, 153, 155, 156, 157.

†Complete breakdown not available.

‡Refs. 4, 5, 18, 26, 27, 35, 48, 54, 55, 56, 57, 58, 59, 69, 70, 74, 75, 78, 85, 91, 94, 98, 102, 106, 107, 109, 110, 111, 112, 113, 114, 125, 126, 133, 141, 147, 149, 150, 158.

Note: All cases in which there was no information as to whether or not there were metastases were placed in the nonmetastatic group.

In order to get a clearer picture as to how the result in these patients compares with that in other series of nonpregnant women, the patients are divided into those with and those without metastases. Of the 201 patients reported to be without metastases before 1941, 21 (10.4 per cent) survived five years and 6 (3 per cent) for ten years, while of the 195 reported after 1941, 59 (30.3

per cent) surivived five years and 42 (21.5 per cent) for ten years. The survival figures before and after 1941 in the cases with metastases are about the same, between 5 and 7 per cent. The total survivals among the 358 patients with metastases are 25 (7 per cent) for five years and 19 (5.6 per cent) for ten years. These subdivisions give a better picture than the gross figures for the 804 cases, 108 (13.4 per cent) surviving five years, and 69 (8.6 per cent) surviving for ten years (Table III).

In an attempt to answer further questions in regard to the relative prognosis of patients treated during pregnancy or nursing, 335 patients are analyzed in regard to the trimester of pregnancy or period of nursing relative to therapy (Table IV). Information in this regard is not available from the large series reported by Harrington,[58 59] Westberg,[150] and other authors. Information is available about 80 patients treated in the first trimester, with 13 (16.3 per cent) five-year survivals, and 6 (7.5 per cent) ten-year survivals; 50 patients were in the second trimester with 4 (8 per cent) five-year survivals and 3 (6 per cent) ten-year survivals; of 62 patients in the third trimester, 6 (9.7 per cent) survived five years and 4 (6.5 per cent) survived ten years; 143 were seen during nursing with 23 (16.1 per cent) five-year survivors and 8 (5.6 per cent) ten-year survivors. These figures are compared with the gross five-year survivals for the entire group of pregnant and nursing patients (13.4 per cent) and the ten-year survivals for the whole group (8.6 per cent).

TABLE IV. RELATIVE PROGNOSIS OF CARCINOMA OF THE BREAST IN PREGNANCY OR NURSING BY TRIMESTERS OF PREGNANCY, COMPARED TO THE PREGNANCY OR NURSING GROUP AS A WHOLE

TIME TREATED	NO. OF CASES	FIVE-YEAR SURVIVORS	TEN-YEAR SURVIVORS
First trimester	80	13 (16.3%)	6 (7.5%)
Second trimester	50	4 (8.0%)	3 (6.0%)
Third trimester	62	6 (9.7%)	4 (6.5%)
Nursing	143	23 (16.1%)	8 (5.6%)
Pregnancy and nursing (entire group)	804	108 (13.4%)	69 (8.6%)

Thirty-six cases have now been reported in the literature with sufficient detail to be considered permanently arrested. These include the 17 cases previously reported from the literature, 13 reported by Harrington to have survived twenty years or longer, 2 reported by McLelland[91] to have survived fourteen and sixteen years without recurrence, 2 reported by Geschickter[48] to have survived 12½ and 20 years without recurrence, and 2 previously reported by me. There is insufficient information about the remaining ten-year survivors following treatment during pregancy or lactation to state whether or not they were cured.

Survival of Patients Treated for Carcinoma of the Breast Prior to Pregnancy or Lactation

As I[151] previously reported, among 12 patients who became pregnant subsequent to treatment for carcinoma of the breast, 6 survived 9, 11, 13, 16, 22, and 31 years without evidence of recurrence, while 2 others died after 16 and 17 years from distant metastases. The total cases from the literature now number 268, with 157 (59 per cent) five-year survivals, and 125 (47 per cent) ten-year survivals. Of the 194 patients without metastases, 124 (64.6 per cent) survived five years and 98 (51 per cent) ten years, while, of the 74 patients with metastases, 32 (43.8 per cent) survived five years and 26 (34.6 per cent) survived for ten years (Table V).

TABLE V. SURVIVAL OF PATIENTS TREATED FOR CARCINOMA OF THE BREAST PRIOR TO PREGNANCY*

	WITHOUT METASTASES			WITH METASTASES			TOTAL		
		SURVIVALS			SURVIVALS			SURVIVALS	
	NO. OF CASES	5 YEARS	10 YEARS	NO. OF CASES	5 YEARS	10 YEARS	NO. OF CASES	5 YEARS	10 YEARS
Articles in literature 1866-1953†	186	117	91	70	31	26	256	149	118
White[151] 1954	8	7	7	4	1	0	12	8	7
Total	194	124 (64.6%)	98 (51%)	74	32 (43.8%)	26 (34.6%)	268	157 (59%)	125 (47%)

*All cases in which there was no definite information as to whether or not metastases were present were placed in the group of nonmetastatic patients.

†Refs. 1, 4, 7, 8, 10, 17, 18, 21, 24, 36, 40, 43, 45, 46, 50, 52, 56, 57, 58, 59, 60, 68, 72, 74, 75, 77, 80, 81, 84, 87, 92, 97, 98, 99, 109, 110, 121, 122, 124, 126, 134, 137, 139, 142, 143.

Effect of Abortion on the Course of Carcinoma of the Breast in the Pregnant and the Nursing Woman

Of the 166 patients whose carcinoma of the breast was complicated by pregnancy and whose pregnancy was aborted, 78 could be analyzed in detail. Of the 78 cases which could be analyzed, 24 patients had coincidental treatment of breast carcinoma and pregnancy terminated by abortion, with an average survival of 30.6 months, 7 five-year survivors and one ten-year survivor. Of the 54 patients who became pregnant subsequent to treatment of the breast carcinoma, 9 survived five years and 2 for ten years, while there was an average survival of 48.2 months.

These 78 patients should be further analyzed with regard to the presence of metastasis at the time of breast carcinoma. Forty-five without metastases at the time of treatment, whether before or simultaneously with pregnancy, survived an average of 62.9 months, with 10 five-year survivors and 3 ten-year survivors. Thirty-three with metastases survived an average of 26.3 months, with 3 five-year survivors and no ten-year survivors.

Westberg reported that 29 of 260 pregnancies in his 224 carcinoma patients were interrupted. He states that a calculation of death risk in this group yields no information as to whether or not abortion influences the course favorably or unfavorably. Adair stated that 34 of 59 patients with operable breast cancer treated during pregnancy or before pregnancy survived five years. Sixteen of the 23 pregnancies were aborted and 11 of his 25 patients who did not have abortions survived five years. Of 12 patients with axillary metastases, who had abortions, 8 survived five years, while, of 12 who did not have abortions, 3 survived five years. Adair does not differentiate in his articles between the patients treated coincidentally with pregnancy or lactation, who have a relatively poor prognosis, and those treated afterward, who have a relatively good prognosis.

Comment

A group of 1,375 cases of carcinoma of the breast complicated by pregnancy has been collected from 144 articles published in the world literature. The largest series to date have been those reported by Harrington[58, 59] from the Mayo Clinic and Westberg[150] from the Radiumhemmet in Stockholm (Table I). A moderate amount of clinical information is available about 1,073

of these patients, sufficient to answer most questions in regard to the 268 who became pregnant subsequent to their treatment. In 335 of 804 cases collected of carcinoma concurrence with pregnancy or nursing, the information is sufficient to answer questions as to the trimester of pregnancy or nursing. The age is known in 751 patients to average 35.8 years. The delay from the doctor's examination for tumor to treatment averaged 3.1 months in 521 patients. There were about 3 cases of pregnancy seen per 100 carcinomas of the breast, and about 3 carcinomas of the breast seen per 10,000 pregnancies. It appears that conclusions in regard to the prognosis of breast cancer and pregnancy will have to be drawn for some time from such small series as these, collected from a number of sources.

The survival rates for the patients treated prior to pregnancy are comparable to those in cases uncomplicated by pregnancy. A high proportion of the 268 patients, 157 (59 per cent), survived five years from treatment, while 125 (47 per cent) survived ten years. Of the 194 patients without metastases, 124 (64.5 per cent survived five years and 98 (51 per cent) survived ten years. Seven of the 8 patients in the series previously reported by me survived ten years, as did 62 of 67 in the experience of Harrington at the Mayo Clinic. Thirty-two of the 74 patients with metastases (42.3 per cent) survived five years and 26 for ten years (34.6 per cent), while none of my 4 patients with metastases survived ten years and only 20 of the 40 patients collected by Harrington were alive after ten years. On the basis of this evidence, the average patient should probably be allowed to have pregnancies subsequent to treatment for carcinoma of the breast. The survival rate does not appear to be appreciably altered by this event.

The situation in regard to patients treated for carcinoma of the breast coincidentally with pregnancy or nursing is much less favorable, with only 13.4 per cent surviving five years and 8.6 per cent for ten years, all 804 cases included. The results in the recent group of patients without metastases are better than before, with 30.3 per cent of the patients reported after 1941 surviving five years and 21.5 per cent surviving for ten years, although only 6.9 per cent of the patients with metastases reported in this period survived five years and 5.2 per cent for ten years. The prognosis for the patient without metastases appears to be over four times as good as for the one with metastases in this period. This is true even when all patients in whom the status as to metastases is unknown are placed in the group without metastases.

In support of the contention that the patients without metastases have a disproportionately greater chance of cure than the group with metastases are the results reported previously by the Mayo Clinic, by Westberg of the Radiumhemmet, and by me. Two of five patients with metastaess in my series and 18 of 23 (78.2 per cent) from the Mayo Clinic survived ten years, as did 63.2 per cent of the patients with no metastases reported by Westberg. On the other hand, none of 5 with metastases in my series survived ten years, only 5 of 103 reported by Harrington from the Mayo Clinic (5 per cent), and 7.3 per cent of the patients reported by Westberg survived ten years. The

difference between the survivals in the groups with and without metastases is very marked. The prognosis may be somewhere between 5 and 20 times as poor in the patients with metastases and in the patients without metastases, as opposed to the usual ratio of between 2 and 3 times. For this reason, delay in treatment in the pregnant or nursing woman is a much more serious factor in determining prognosis than in the uncomplicated carcinoma of the breast.

The lower survival rate noted in the second and third trimesters of pregnancy as opposed to the first trimester and the nursing period may in part be due to a tendency on the part of the obstetrician or surgeon to delay treatment until term in cases appearing during the latter part of pregnancy. In view of the much less favorable prognosis in the patient with metastases, this delay seems inadvisable. Undoubtedly pregnancy and nursing have an unfavorable influence on breast carcinoma which can be met only by a more vigorous approach to the disease during this period. Biopsy should be taken of the wall of inflammatory lesions at the time of incision and drainage in order to assure the surgeon or obstetrician that carcinoma is not present. Masses should be biopsied promptly, if they persist. With earlier treatment, more cases of carcinoma of the breast will be arrested.

Abortion cannot be shown to have a clear effect on the course of carcinoma of the breast complicated by pregnancy. The 108 patients in whom abortion occurred were not a sufficient number to furnish a definite conclusion in this regard.

Conclusions

1. Carcinoma of the breast complicates pregnancy about three times per 10,000 pregnancies, while pregnancy complicates breast carcinoma about three times per 100 breast carcinomas.

2. Only 1,375 cases of carcinoma of the breast complicated by pregnancy have been reported in the world literature, many of these reports being fragmentary.

3. The gross five-year survival rate (59 per cent) and ten-year survival rate (47 per cent) of patients treated for carcinoma of the breast who became pregnant later is comparable to or better than the gross survival rates of patients without pregnancy.

4. Although the summation of reports of ten-year survivals with coincidental treatment of carcinoma of the breast and pregnancy indicates only 8.6 per cent survivals, 21.5 per cent of the patients without metastases reported since 1941 survived ten years, including 2 of 5 reported by me, 78.2 per cent of those reported by Harrington, and 63.2 per cent of those reported by Westberg.

5. The patients with metastases treated during pregnancy or during nursing have from 5 to 20 times as poor a prognosis as those without metastases.

6. The ages of 751 patients averaged 35.8 years.

7. The delay between the doctor's examination for tumor and the treatment averaged 3.1 months in 521 patients.

8. The prognosis in patients treated for the first time during the second and third trimesters of pregnancy appears to be less favorable than for those treated during the first trimester or during lactation. The poorer prognosis in this group of patients may be the result of a wish on the part of both physician and patient to delay treatment during the latter part of pregnancy.

9. No clear benefit can be demonstrated from abortion to the patient with breast carcinoma complicated by pregnancy.

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A CLINICAL EVALUATION OF 25 CASES TREATED WITH TERRAMYCIN INTRAMUSCULAR*

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TERRAMYCIN hydrochloride† is not a new antimicrobial agent any longer. Its broad spectrum of bactericidal action is well known and has been previously reported by many workers.[1-4] The oral form of this drug has been clinically tried and proved. Toxic reactions, blood levels, and limitations of use are all well known. It is not the purpose of this report to evaluate the drug Terramycin, but to help determine whether or not local administration of the crystalline hydrochloride is feasible. To be able to administer a broad-spectrum antibiotic by the intramuscular route has not yet been clinically possible until the advent of Terramycin Intramuscular (T.I.M.). Such a route of administration would prove a valuable one in our armamentarium of drugs for parenteral use where necessary, when oral therapy is not practical nor possible, as in gastrointestinal obstruction, lack of patient cooperation, i.e., coma, postoperative shock, nausea, and other contraindications to oral therapy.

The accepted dose recommended by previous workers and adhered to in this report was 100 mg. twice a day. Higher dosage may be used but this has been found to be an optimum dose for most acute infections of mild and moderate severity. It has been recommended that 200 mg. doses every 8 to 12 hours be used for severe infections.

It has already been shown that 100 mg. of Terramycin Intramuscular will produce a blood level equivalent to 500 mg. of the oral drug.[5] These levels are maintained for at least 9 hours, reaching a peak between 4 and 6 hours after administration. Therapeutic levels of over 1.5 mg. per milliliter are reached by 2 hours and a height of 2.5 mg. by 4 hours. These levels have been found to parallel the blood levels of a 500 mg. oral capsule.

Daily intramuscular doses of above 200 mg. may be used but this report included only cases treated with 100 mg. twice a day, with a total of 200 mg. in 24 hours.

Administration

The drug was supplied in 250 mg. vials in the form of hydrochloric salt with the addition of magnesium chloride to improve local tissue tolerance. Also included in the vial was 2 per cent procain hydrochloride to alleviate pain and discomfort at the site of injection.

*Presented at a meeting of the Memphis and Shelby County Medical Society, Jan. 5, 1954.

†Terramycin Intramuscular contains 100 mg. oxytetracycline hydrochloride and 50 mg. procaine hydrochloride, 100 mg. of sodium glycinate, 100 mg. of polyvinyl pyrrolidone and 0.2 per cent sodium bisulfite as a preservative and is manufactured by Pfizer Laboratories.

Sterile water was used as a diluent in these 25 cases. Physiologic saline will be used in later cases.

The drug was administered with care through 22 gauge needles, into the lateral aspect of the thigh muscles. Care was observed to avoid injection into fat and subcutaneous tissues where sequelae are reported to be more prominent. Each injection totaled 100 mg., utilizing 50 mg. to 1 c.c. diluent, or a 2 c.c. total injection.

TABLE I

CASE NO.	INITIALS AND CHART NUMBER	NUMBER OF HOSPITAL DAYS	NO. OF MORBID DAYS AFTER START OF DRUG	TOTAL NUMBER OF INJECTIONS	PAIN	DIAGNOSIS AND REMARKS
1	M. M.	3	2	6	None	Infected incomplete abortion
2	E. T.	7	0	7	With 6th shot	Adominal hysterectomy, salpingo-oophorectomy, appendectomy, multiple fibroids
3	V. S.	10	0	8	With 7th shot	Cesarean section, wound dehiscence, secondary closure
4	D. B.	7	0	4	None	Low cesarean section, 30 hours, trial labor, ruptured membranes
5	J. J.	4	0	2	None	6 months premature delivery of stillborn infant with shock and hemorrhage, manual removal of retained placenta
6	E. B.	7	0	7	With 5th shot	Left tuboovarian abscess subacute, surgically removed
7	B. R.	5	1	4	None	Pyelitis of pregnancy
8	B. R.	4	0	4	With 3rd shot	Incomplete abortion
9	R. S.	7	0	14	None	Vaginal hysterectomy (medicine neglected to be discontinued)
10	V. R.	8	5	5	With 3rd shot	Pyelitis. Poor response to Terramycin. Sulfadiazine used
11	M. W.	4	1	3	None	Acute salpingitis
12	C. P.	10	2	14	With 2nd shot	Third-degree tear. Rectal contamination
13	K. M.	5	1	6	With 3rd shot	Third-degree laceration
14	M. D. 45197	8	0	5	None	Placenta previa. Vaginal delivery, ruptured membranes 48 hours
15	C. M. C. 43252	6	0	12	None	Pyelitis
16	J. K. 45602	7	0	6	None	Secondary closure of episiotomy with hematoma
17	D. B. 45700	9	5	6	With 4th shot	Pyelitis. Drug changed to sulfadiazine
18	L. S. 45764	7	0	10	None	Third-degree laceration
19	M. W. 46739	5	0	6	None	Third-degree laceration
20	G. B. 45952	8	0	13	With 6th shot	Third-degree laceration
21	M. D. 46051	5	2	6	None	Pyelitis of pregnancy
22	W. N. 47132	7	0	5	With 3rd shot	Third-degree laceration
23	B. G. 47026	6	0	4	With 2nd shot	Ruptured corpus luteum with hemoperitoneum, shock
24	E. C. 47093	6	2	7	None	Postpartal sepsis. Acute endometritis
25	G. M.	4	0	8	None	Cesarean section with ruptured membranes and repeated vaginal examinations

The drug was administered in the 25 cases in Table I. All patients were told it was Terramycin in intramuscular form, though none were told it was a clinical study. All were asked to report any local reactions of unusual nature to delineate clearly the amount of discomfort they experienced, and to report any reactions of a systemic or general nature.

Reactions

In the 25 cases, 170 intramuscular doses of 100 mg. of Terramycin were given by various registered nurses. There was no reported deep abscess formation, skin discoloration, or subcutaneous skin reaction at the site of injection. There were numerous complaints of pain which are further tabulated. In no case was a report made of generalized skin reaction, and no unusual systemic reaction was recorded.

As mentioned, the most distressing difficulty encountered was the complaint of pain. In 25 cases 44 per cent suffered pain at the site of injection. At no time was the pain severe enough to merit discontinuing the drug. There were 2 patients who received a total of 14 shots each, one a total of 13, and another a total of 10. In none of these patients was the pain unusual, though it was present after the third shot in 3 of these cases. In all cases where pain was experienced, it was found the discomfort disappeared 24 to 48 hours after the drug was discontinued. If the number of injections is greater some residual soreness may remain for a longer period of time.

Discussion of Cases

The 25 cases were chosen at random from the service here at U. S. Naval Hospital, Memphis, Tennessee. In each instance, infection was known to be present by clinical manifestation, or could be expected from known contamination during delivery or surgery.

Morbidity was defined as a temperature of 100.4° F. for two successive days, or over 101.° F. for any one day, excluding the day medication was started.

In 15 of the 25 cases, there were no morbid days after the start of the drug. Of the 10 patients who did show morbidity, only two were found to be resistant to Terramycin therapy. These two had pyelitis. Both responded to sulfadiazine.

The total number of morbid days for the 25 patients in the study was 21. The total number of hospital days was 159.

Though this series is yet small, it is believed the use of intramuscular Terramycin will lower morbidity appreciably in the cases usually classified as potentially infected ones, i.e., those with ruptured membranes of long duration, rectal and vaginal surgery, secondary surgical procedures, and manual invasion of the uterus. This will, in turn, reduce the number of *hospital days* a group of patients of this type will incur. This is a prime consideration to all of us and to the private patient, with our present high cost of hospitalization.

In these 25 cases, none were hospitalized over 10 days. The average for the group was 6.3 days.

Comments

From the observations made in this small series, it is believed Terramycin Intramuscular will prove a valuable addition to the parenteral antibiotics in the broad-spectrum group. The intramuscular route of administration of Terramycin is much easier than the previously developed intravenous route and is apparently most efficacious in acute infections of mild and moderate severity.

The use of Terramycin in surgery and obstetrics should become general after consideration of the clinical results in these 25 cases. The only undesirable factor found in administration of this new preparation is the pain experienced at the site of injection. Forty-four per cent of the patients who received the drug complained of pain of varying degrees of severity and until this pain is eliminated or reduced to a smaller percentage it may prove a retarding factor in the acceptance of the intramuscular route of administration of Terramycin.

Conclusions

1. Terramycin can be safely administered intramuscularly.

2. A dose of 100 mg. twice a day will adequately control most acute infections of mild and moderate severity.

3. Pain at the site of injection is the only apparent limitation of use of Terramycin Intramuscular. There were no systemic reactions noted in this series.

4. The amount of pain at the injection site, though a problem at present, does not prohibit the use of the intramuscular preparation where necessary.

I wish to express my appreciation to Harry Seneca, M.D., of the Pfizer Laboratories for his assistance in the preparation of this report. In addition I wish to express my gratitude to the nursing personnel of the U. S. Naval Hospital, Memphis, Tennessee, and to Mrs. Helen Meadows and Mrs. Alice Hulseberg for their efforts in the preparation of this manuscript.

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VASCULAR TUMORS OF THE UTERUS

I. Benign Vascular Tumors

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ALTHOUGH benign blood-vessel neoplasms are fairly common and are rather widely distributed throughout the human body, they are relatively rare in the uterus. This is somewhat surprising in view of the rich vascularity of that organ, particularly when the cyclic changes of the blood vessels associated with menstruation and pregnancy are considered. Only 128 cases of vascular tumors of the uterus have been reported, out of the very large number of uteri examined yearly.

Considerable confusion about these neoplasms arises from the multiplicity of names used to describe an identical tumor, and because of failure to differentiate between the terms used to describe benign and malignant varieties of some of these new growths.

An opportunity to study vascular neoplasms of the uterus arose with the discovery of 10 cases at the Jewish Hospital of Brooklyn, collected over a period of eighteen years. Together with the cases previously reported, 138 cases were thus made available for analysis and classification. Increasing awareness by gynecologic pathologists of the existence of these uterine tumors will undoubtedly lead to recognition of many more cases.

At least 15 different names have been applied to tumors of this group, many to identical neoplasms. In several instances, in the literature, no distinctions were made between benign and malignant varieties of the same type of new growth. In order to achieve some measure of conformity of nomenclature and to obtain a clearer understanding of vascular tumors of the uterus, the following classification, based on histological characteristics of each member of this group of neoplasms, is proposed.*

BENIGN VASCULAR TUMORS (ANGIOMAS)

Blood-vessel origin:

1. Hemangioma
   - Capillary hemangioma
   - Cavernous hemangioma
   - Hemangiomatosis
2. Angiomyoma
3. Hemangioendothelioma (benign)
4. Hemangiopericytoma (benign)

Lymph-vessel origin:

1. Lymphangioma
2. Lymphangiocystic fibroma

*This classification was reviewed and found acceptable by both Drs. Arthur Purdy Stout and Arthur T. Hertig, who have long been interested in the study of vascular tumors.

MALIGNANT VASCULAR TUMORS (ANGIOSARCOMAS)

Blood-vessel origin:

1. Hemangioendothelioma (malignant)
2. Hemangiopericytoma (malignant)
3. Kaposi's sarcoma

Lymph-vessel origin:

1. Lymphangiosarcoma

Histogenesis and Morphology

Embryologically, the earliest vessels to be formed develop from "blood islands" in the extraembryonic mesoderm. They begin as unconnected solid cords which become canalized on further differentiation, anastomosing later to form a vascular network of capillaries. Failure of the vascular channels to unite results in an independently developing group of isolated blood vessels, forming hemangiomas.

Subsequent development of a vascular tumor is the result of an apparent outgrowth of solid buds of endothelium from previously formed vessels, as in granulation tissue. Such growths probably arise in situ, similarly to the formation of embryonic capillaries and, following development of lumina in the endometrial buds, they join the general circulation.

The two large groups of angiomas, as classified, are: (1) those arising from blood vessels, and (2) those arising from lymph vessels.

Benign Angiomas of Blood-Vessel Origin

Hemangioma.—Congeries of endothelium-lined blood vessels compose this tumor, which may vary in size from a pea-sized nodule to a neoplasm measuring 25 cm. or more. Submucous tumors may be pedunculated, resembling a polyp or fibroid of the uterus. Intramural hemangiomas often are localized, but they may also be diffuse, extending over large areas of myometrium. Focal hemangiomas impart a hemorrhagic appearance, whereas diffuse tumors cause the uniformly enlarged uterus to take on a purplish hue (Fig. 1). Softening of the uterus often suggests pregnancy. On gross section, the uterine wall presents a honeycombed appearance, with marked variation in size of the endothelium-lined sinuses. Notable decrease in size of the uterus follows surgical removal as blood escapes from the innumerable sinuses of the tumor.

Hemangioma of the cervix is similar to that of the corpus, and may also be either focal or diffuse.

Capillary hemangioma is the most common variety of hemangioma of the uterus and is often multiple. Small, narrow vascular channels lined by a single flat layer of endothelium are surrounded by variable amounts of fibrous connective tissue (Fig. 2, *a* and *b*). The neoplasm is distinguished by the presence of thicker-walled newly formed capillaries, which differentiates it from normal tissues with passive congestion (Fig. 3). Occasionally areas of hyalinization of the vessels may be seen (Fig. 4).

Cavernous hemangioma differs from capillary hemangioma in that the majority of vessels comprising the tumor are widely dilated, with only thin layers of intervening fibrous connective tissue (Fig. 5).

Angiomyoma.—This tumor is composed of proliferating blood vessels and smooth-muscle bundles arranged in whorls. It is benign and varies in size from a few millimeters to 22 cm. or more in diameter, greatly resembling ordinary uterine fibromyomas. Subserous, intramural, and submucous varieties of the

TABLE I. REPORTED CASES OF HEMANGIOMA OF THE UTERUS

AUTHOR AND YEAR	AGE	PARITY	SYMPTOMS				LOCATION		THERAPY		REMARKS
			MENOMETRORRHAGIA	POSTMENOPAUSAL BLEEDING	PAIN		SUBMUCOUS	INTRAMURAL	CURETTAGE	HYSTERECTOMY	
Krull (1820)	No information available										
Duparque (1826)											Uterine rupture, pregnancy. Diffuse tumor
Kiwisch (1851)	No information available										
Cruveilheir (1856)	No information available										
Lee (1864)	29	iii	+					+		+	Diffuse tumor
Klob (1864)		M						+		+	Bluish-colored tumor
Boldt (1893)	37	0	+					+		+	In right cornu; 2 × 4 cm.
Halban (1904)	26	0	+					+	+	+	Perforation of pregnant uterus with curette
					+						
Dorsett (1911)										+	
(1911)										+	
Poucher (1911)										+	
Bauereisen (1912)		iii						+			Spontaneous rupture of term uterus during labor
Boks (1917)	33	ii	+				+			+	Polypoid tumor; 6 cm.
Meyer (1924)	62			+			+		+		Tumor in curettings
(1925)	47	vi	+					+		+	2 × 3 cm.
(1925)	49	i	+				+			+	2 × 3 cm.
(1925)	44	ii	+					+		+	5 × 6 cm.
(1925)	47		+					+		+	2 × 4 cm.
Vital (1927)			+				+				Cavernous type of tumor
Neumann (1927)	38	ii	+				+			+	Polypoid tumor
Von Ligner (1928)	39	0						+		+	Uterus enlarged, soft
Neumann (1929)	50	ii		+				+		+	"Small" tumor
(1929)	42	iv	+					+		+	"Small" tumor
Horgan (1930)	46	iv	+				+			+	Dark red, on anterior wall
Bartsch (1930)	53	iii	+				+			+	
Klee (1932)	54	0	+					+		+	Diffuse; 25 × 20 × 14 cm.
Dutta (1932)	31	iv	+				+			+	Bleeding tumor vessel; shock
Pusch (1932)	33	0			+		+			+	
Vonteck (1934)							+				No other details
Papin (1938)	20	0	+					+		+	Diffuse, with rapid growth of tumor
Ratzenhofer (1940)	46	i	+					+		+	
Levy-Solal (1944)	40	0	+				+		+	+	Hysterogram revealed left cornual tumor
Strickler (1947)	45	i	+					+		+	Pulsating uterus, 4 months' size. Considered inoperable 7 years before
Englund (1949)		v						+		+	Rupture of term uterus
MacDonald (1950)	27	0			+			+		+	Diffuse tumor
Marsh (1950)	50	iii	+		+			+		+	Polypoid tumor; 9 × 6 cm.
Malpas (1952)	34	ii	+					+	+	+	Hemorrhage after curettage
Stout (1953)	No information available										Cavernous tumor
(1953)	No details available										Involvement of uterus, vulva, and broad ligament
Authors	73	M					+				Autopsy. 2 cm. diameter
	65	M						+			Autopsy. 2 cm. diameter
	61	M						+			Autopsy. 1.5 cm. diameter

TABLE II. HEMANGIOMAS OF THE CERVIX

AUTHOR AND YEAR	AGE	PARITY	SYMPTOMS: MENOMETRORRHAGIA	SYMPTOMS: POSTCOITAL BLEEDING	SYMPTOMS: PAIN	TYPE: DIFFUSE	TYPE: POLYPOID	OPERATION: BIOPSY OR AMPUTATION	OPERATION: POLYPECTOMY	OPERATION: HYSTERECTOMY	REMARKS
Wild (1891)	27	0	+	+	+		+		+		Bluish-red tumor
(1891)		0	+				+		+		Bluish-red tumor
Falk (1898)	24	iii					+		+	+	Vaginal hysterectomy
Di Bernardo (1923)	26	ii				+				+	
Machado (1941) and Junqueira (1942)	31	ii	+	+		+		+			Port-wine color. All these tumors were thought to be malignant
(1942)	48		+	+		+		+			
(1942)		xiii	+	+		+		+			
(1942)			+	+		+		+			
(1942)	45		+	+		+		+			
(1942)			+	+		+		+		+	
Tyrone (1947)	No details available	i									Found during routine microscopic section
(1947)						+				+	Bluish tumor
Weed (1948)						+				+	Port-wine color, faded on pressure
McNabb (1949)								+			
Nobrega (1949)	25	i	+	+		+					
Authors	53	iv				+			+		
	35	ii		+		+	+				

TABLE III. HEMANGIOMAS OF THE PELVIC SUPPORTING STRUCTURES

AUTHOR AND YEAR	AGE	PARITY	SYMPTOMS	OPERATION	FINDINGS	END RESULT
Harie (1906)	35	–	Not stated	Laparotomy	Fluctuating mass anterior to uterus, contained old blood	Mass incised and patient died from hemorrhage
Pantzer (1911)	26	ii	Abdominal pain, mass, menorrhagia, hematuria	Ligation of right uterine and ovarian vessels	Involvement of right half of uterus, broad ligament, and bladder	Living and well 1½ years, postoperatively
Wright (1926)	38	v	Pelvic mass	Hysterectomy	Right broad ligament and right half of uterus	Living and well
Frank (1930)	35	0	Abdominal pain and enlargement	Hysterectomy	Right broad ligament anterior of uterus to bladder	Left salpingo-oophorectomy 6 years before, for hemangioma of left broad ligament. Laparotomy for recurrence in left side 2 years after present operation. Inoperable, given x-ray and was asymptomatic 2 years later

TABLE IV. ANGIOMYOMAS

AUTHOR AND YEAR	AGE	PARITY	LOCATION				OPERATION		REMARKS
			SUBMUCOUS	INTRAMURAL	SUBSEROUS	INTRALIGAMENTOUS	MYOMECTOMY	HYSTERECTOMY	
Virchow (1867)				+				+	
Mermet (1896)	50	0			+			+	
Höhne (1901)					+			+	
Oulie (1901)	26			+				+	
Michel (1903)	45	iii		+				+	Very rapid growth of tumor
Audibert (1903)	50		+				+		Vaginal myomectomy
Reder (1904)				+				+	Severe hemorrhage during myomectomy necessitated hysterectomy
Bell (1906)	41	0		+				+	Tumor was cystic to palpation
Kelly and Cullen (1909)				+				+	Tumor measured 12 × 10.5 cm.
				+				+	Diameter 6 cm.
					+			+	Dark red; 12 × 9 × 7 cm.
	45			+				+	22 × 20 × 15 cm.
Shaw (1913)	65			+				+	Severe abdominal pain
Hirschberg (1924)	64	iv	+					+	Postmenopausal bleeding
Tauber (1925)	47		+					+	Vaginal hysterectomy
Ehnmark (1928)	31	0	+	+			+		
De Josselin de Jong (1928)	No details available								
Erede (1928)	38	0		+				+	"Fibroids" appeared reddish
Mandelstamm (1929)	25						+		
Neumann (1929)	41		+				+		Vaginal myomectomy; 4 × 3 cm.
Lockyer (1930)				+				+	
				+				+	
					+			+	Sarcomatous changes noted
Meyer (1930)	35					+		+	6 cm. in diameter
Stoeckel (1930)	52	0				+		+	
Ascheim (1930)	53	xi		+				+	
Gupta (1931)	40	i				+		+	"Size of fetal head"
	48		+						Treatment not stated
			+						Size of "melon"
	40	vi			+			+	Pulsating tumor; size of "fetal head"
Johns (1933)	57							+	
Eiserth (1934)	48		+						Found at autopsy
Von Orsos (1934)	45							+	
Gardner (1940)	40	0	+					+	Sarcomatous change; died in 2 years
	36	i	+					+	Vaginal hysterectomy. Sarcomatous change; living 2½ years postoperatively
	41	0	+					+	Sarcomatous change
Gnassi (1941)	39	ii				+		+	Sarcomatous change
Sammartino (1947)	36		+					+	Polypoid tumor
Schinkele (1947)	44	0	+					+	Vaginal hysterectomy
Stout (1953)	4 cases; no data available.								One was sarcomatous
Authors	35	ii			+			+	Measured 13 × 12 × 5 cm.
	53	iii		+				+	8 cm. in diameter
	22	0	+				+		

TABLE V. CAVERNOUS LYMPHANGIOMAS

AUTHOR AND YEAR	AGE	PARITY	PAIN	INTRAMURAL TUMOR	HYSTERECTOMY	REMARKS
Umeda (1935)	77			+		Autopsy specimen; right cornu
Nicod (1938)	20			+	+	Diffuse tumor
Authors	42	0	+	+	+	Diffuse tumor

TABLE VI. LYMPHANGIOCYSTIC FIBROMAS

			SYMPTOMS				LOCATION				
AUTHOR AND YEAR	AGE	PARITY	MENOMETRORRHAGIA	ABDOMINAL PAIN	RAPID GROWTH		INTRAMURAL	SUBSEROUS	INTRALIGAMENTOUS	HYSTERECTOMY	REMARKS
Reuter (1915)	28	i		+	+		+			+	On posterior wall
Meyer (1925)	40	M					+			+	Posterior wall; 5 × 4 cm.
Von Zakrzewski (1925)							+			+	Left horn of uterus
Isbruch (1927)	44	i	+				+			+	Received x-ray for bleeding 1 year prior to hysterectomy
Neumann (1929)	37	0		+			+			+	28 × 19 × 15 cm.
Meyer (1930)	46						+			+	Anterior wall; size of "apple"
Wolff (1930)	41						+			+	
Baumgart (1930)	30		+				+			+	
Mackenrodt (1930)	69						+			+	Size of "man's fist"
Kaufmann (1931)	55		+				+			+	
	45	0	+				+			+	Size of "man's head"
(1932)							+			+	Size of "hazelnut"
Dworzak (1932)	45	iii	+	+			+			+	Size of "child's head"
Motyloff (1932)	56	i		+				+		+	Died several months later with "spindle-cell sarcoma"
	41	i		+					+	+	
Muschick (1932)	41	ii	+				+			+	
	44	iii		+			+			+	4 × 3 × 4 cm.
Finger (1932)	28		+	+	+		+			+	Had been suspected of pregnancy
Brenner (1934)	34	0	+	+			+			+	24 × 16 × 14 cm.
Pahl (1934)	42	i	+				+			+	12 × 10 × 8 cm.
De Meuron (1935)	31	iv	+	+			+			+	Size of "orange"
Krenzer (1935)	58						+			+	
Limburg (1942)	55	iii	+					+		+	Size of "head." Living and well 19 months postoperatively
	35	i	+	+	+		+			+	13 × 12 × 6 cm. Died several months postoperative with metastases from an associated lymphangioendothelioma
Plaut (1946)	50	iv	+							+	Vaginal hysterectomy for lymphangiocystic fibroma of cervix
Authors	49	iv		+					+	+	7 cm. diameter

TABLE VII. LOCATION OF LESION IN 138 CASES OF BENIGN VASCULAR NEOPLASMS OF THE UTERUS

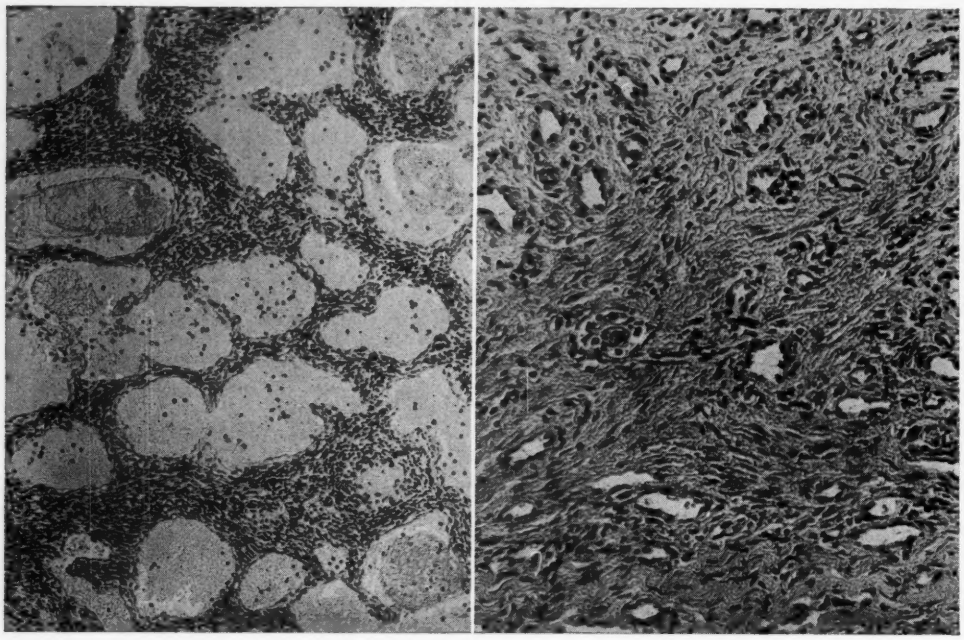
SITE	HEMANGIOMAS			ANGIO-MYOMAS	LYMPHAN-GIOMAS	LYMPHAN-GIOCYSTIC FIBROMAS
	UTERUS	CERVIX	PELVIC SUPPORTING STRUCTURES			
Cervix.—						
Diffuse		13				1
Polyp		3				
Submucous	13			14		
Intramural	21			15	3	21
Subserous	0		1*	6		2
Intraligamentous	0		3	4		2
Not stated	8	1		8		
Total	42	17	4	47†	3	26

*Neoplasm was between uterus and bladder.
†One angiomyoma was both subserous and intramural.

tumor have been described (Table VII). At laparotomy the markedly increased vascularity of subserous tumors imparts a cyanotic appearance and a notable pulsation in the area of the growths. The presence of a pseudo-capsule about the neoplasm allows a ready enucleation of the tumor, which, on cut section, exhibits typical whorls of smooth-muscle bundles. Scattered amid the bundles are dark-blue focal areas of blood-filled vessels, most notable about the center of the new growth, which greatly resemble a honeycomb. The vessels are closely packed and vary markedly in size. Cystic degeneration is often present, and the neoplasm may undergo sarcomatous degeneration as occasionally occurs in ordinary uterine myomas.

Fig. 1.—N42-72. Intramural hemangioma of the uterus encroaching upon the endometrial cavity.

Microscopic examination reveals the tumor to be made up of angiomatous areas and whorls of smooth muscle (Fig. 6). The blood vessels vary in size and may be either thin- or thick-walled, with a uniform and well-preserved endothelial lining (Fig. 7). In the larger vessels, however, hyaline degeneration



A. *B.*

Fig. 2.—*A*, N42-73. Hemangioma of the uterus. Abundant stroma, with round cell infiltration, (Hematoxylin and eosin. ×150; reduced ⅕.)
B, SP.53-3266. Capillary hemangioma of the cervix. (Hematoxylin and eosin. ×150; reduced ⅕.)

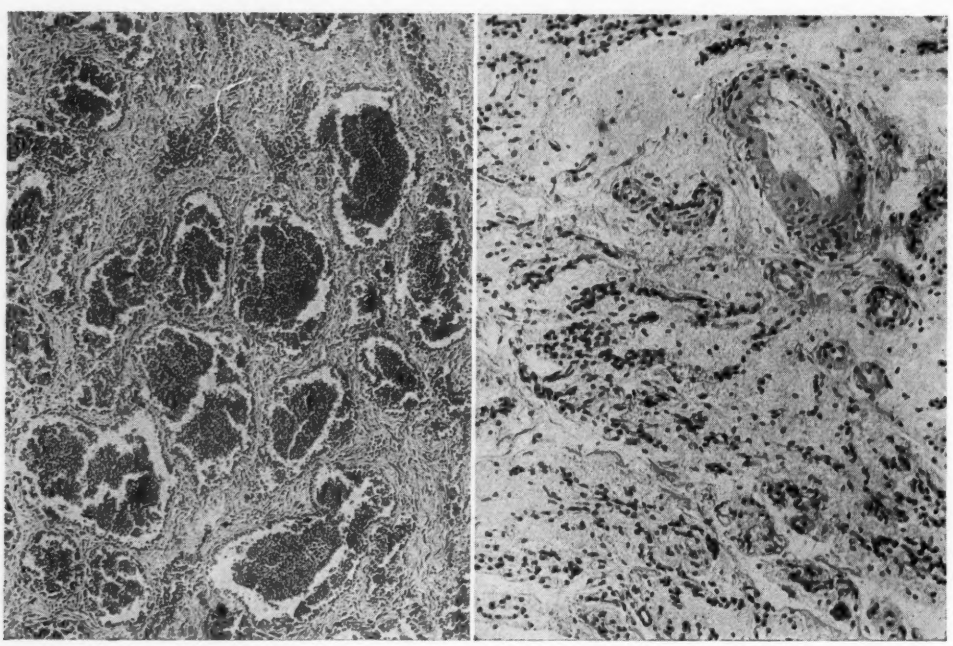


Fig. 3. Fig. 4.

Fig. 3.—S.P.48-1949. Postpartum cervix: marked dilatation and congestion of blood vessels. (Hematoxylin and eosin. ×150; reduced ⅕.)
Fig. 4.—N42-73. Hemangioma of the uterus; hyalinization of blood vessels. (Hematoxylin and eosin. ×150; reduced ⅕.)

of the smooth muscle of the media is often present, as well as areas of hyaline degeneration of the smooth muscle of the tumor, itself. In view of the rich vascularity of the neoplasm, such degeneration is difficult to explain (Fig. 8).

Although angiomyomas so markedly resemble highly vascular uterine myomas, the diagnosis can be readily established by observing the presence of both newly formed, thin-walled capillaries and older blood vessels within the same area of the tumor. The older vessels serve to distinguish the neoplasm from a uterine myoma with passive congestion resulting from torsion, infarction, or circulatory stasis (Fig. 3).

Histogenesis: Angiomyomas originate from embryonic mesodermal elements within the wall of the uterus. The neoplasm develops either from simultaneous proliferation of smooth muscle and vascular elements of primitive mesoderm, or the smooth-muscle component develops from the media of newly formed vessels as in angiomyoma of the skin. At present there is no evidence favoring either of these two concepts.

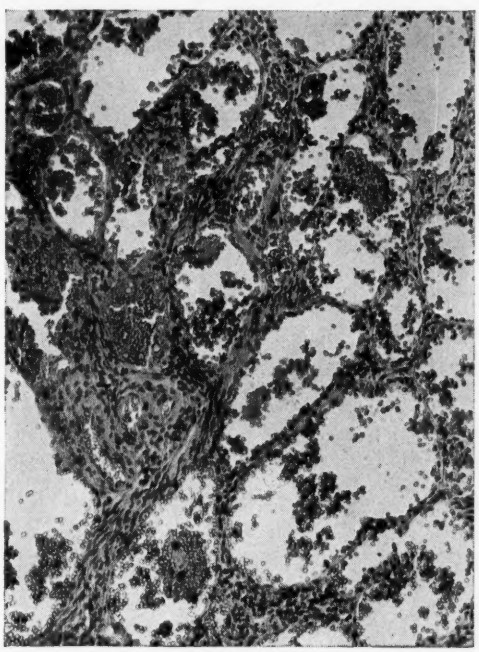


Fig. 5.—N39-218. Cavernous hemangioma; scant stroma and thick-walled new blood vessels. (Hematoxylin and eosin. ×150; reduced ⅙.)

With continued growth of the tumor the central vessels approach the periphery of the neoplasm where they establish communication with the vascular supply of the adjacent myometrium. In ordinary uterine myomas the blood supply enters the tumor *from* the periphery, having been derived from adjacent blood vessels.

Hemangioendothelioma and *Hemangiopericytoma.*—Since both tumors may be either benign or malignant, they will be described under "Malignant Vascular Tumors of the Uterus."

Lymphangioma.—The marked resemblance of lymphangioma, composed of lymph channels, to lymphangiectasia serves to make differentiation exceedingly difficult, and by some pathologists they are considered to be identical. Lymphangioma is rarely found in the uterus. *Simple lymphangioma* is made up of

Fig. 6.

Fig. 7.

Fig. 8.

Fig. 6.—SP.45-5558. Angiomyoma of the uterus. (Hematoxylin and eosin. ×30; reduced ⅕.)
Fig. 7.—SP.45-5558. Angiomyoma of the uterus; cellular stroma and marked vascularity. (Hematoxylin and eosin. ×150; reduced ⅕.)
Fig. 8.—SP.45-5558. Angiomyoma of the uterus; hyalinization of stroma. (Hematoxylin and eosin. ×150; reduced ⅕.)

Fig. 9.

Fig. 10.

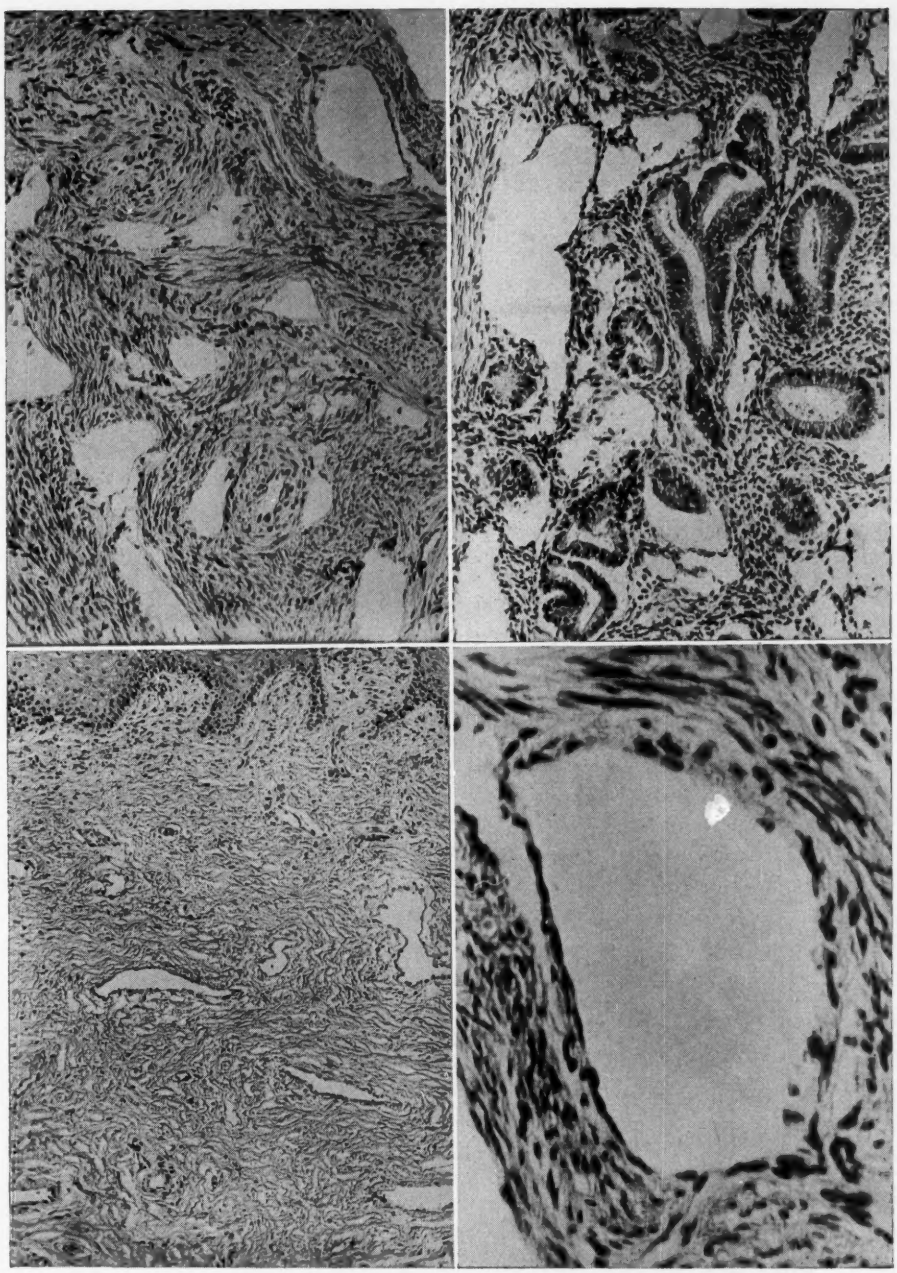


Fig. 11.

Fig. 12.

Fig. 9.—SP.52-4861. Lymphangioma of uterus, involving myometrium. (Hematoxylin and eosin. ×150; reduced ⅙.)

Fig. 10.—SP.52-4861. Lymphangioma of uterus, involving endometrium. (Hematoxylin and eosin. ×150; reduced ⅙.)

Fig. 11.—SP.52-4861. Lymphangioma of uterus involving cervix. (Hematoxylin and eosin. ×150; reduced ⅙.)

Fig. 12.—SP.52-4861. Same tumor as shown in Fig. 10. Higher magnification to demonstrate endothelial lining. (Hematoxylin and eosin. ×400; reduced ⅙.)

Fig. 13. Fig. 14. Fig. 15.

Fig. 13.—SP.48-429. Lymphangiocystic fibroma of uterus. (Hematoxylin and eosin. ×150; reduced ⅙.)
Fig. 14.—SP.48-429. Lymphangiocystic fibroma of uterus. Higher magnification revealing cellularity of fibrous connective tissue stroma. (Hematoxylin and eosin. ×400; reduced ⅙.)
Fig. 15.—SP.48-429. Lymphangiocystic fibroma of uterus; endothelial lining of cystic space. (Hematoxylin and eosin. ×400; reduced ⅙.)

lymph vessels of small and medium caliber; *cavernous lymphangioma* consists of widely dilated lymph vessels separated by delicate or thickened septa. Coagulated lymph may occasionally be present in the larger lymphatics. Small, newly formed lymphatics may be noted in either type of lymphangioma. No cases of *cystic lymphangioma* of the uterus have been reported.

Histogenesis: Lymphangioma arises from mesoderm by budding and proliferation of endothelium, similarly to the formation of angiomas. The case of cavernous lymphangioma, herein reported, involved both the uterus and cervix (Figs. 9-12).

Lymphangiocystic Fibroma.—Numerous lymph vessels in a matrix of highly cellular fibrous connective tissue differentiate lymphangiocystic fibroma from a uterine fibromyoma with lymphangiectatic changes. The tumor varies in size from a small nodule to one that measures 24 cm. or more. The majority average 7 to 10 cm. in diameter. On gross section, a central cavity of varying size is usually exposed, containing a cloudy fluid or blood.

Histologic examination reveals that the solid portions of a lymphangiocystic fibroma consist of highly cellular fibromatous tissue, readily demonstrated by special connective-tissue stains (Figs. 13, 14). Condensation of tissue in some areas of the tumor forms broad bands of collagen. Lymphangiocystic fibroma is differentiated from a uterine myoma by the absence of smooth muscle bundles and the presence of characteristic lymph channels lined by a single layer of endothelial cells (Fig. 15). The fluid pressure within the central cavity of the tumor often causes marked flattening of the endothelial lining or its complete destruction. Mast cells, noted frequently in this tumor, are indicative of its connective tissue structure.

The origin of this neoplasm is still conjectural. It was grouped by Robert Meyer with those tumors resulting from developmental flaws. Lymphangiocystic fibroma is probably the lymph-vessel counterpart of angiomyoma and has its origin from primitive mesoderm, but whereas the solid portion of angiomyoma is formed by smooth muscle, the solid portion of lymphangiocystic fibroma is composed of fibrous connective tissue.

Clinical Picture

Age and Parity.—Although benign vascular tumors of the uterus appear at any age, they are most frequent during the fourth and fifth decades of life. Parity is apparently of little significance (Tables VIII and IX).

TABLE VIII. DISTRIBUTION OF 138 CASES OF BENIGN VASCULAR TUMORS OF THE UTERUS ACCORDING TO AGE OF PATIENT

	HEMANGIOMA					
AGE IN YEARS	UTERUS	CERVIX	PELVIC SUPPORTING STRUCTURES	ANGIOMYOMA	LYMPHANGIOMA	LYMPHANGIOCYSTIC FIBROMA
20-29	4	4	1	3	1	2
30-39	7	2	3	7	0	5
40-49	9	2	0	13	1	11
50-59	4	1	0	6	0	5
60-69	3	0	0	2	0	1
70+	1	0	0	0	1	0
Not stated	14	8	0	15	0	2
Total	42	17	4	46	3	26

Symptoms.—The symptoms are not characteristic, and often benign vascular tumors of the uterus are entirely symptomless (Table X). Vaginal bleeding occurs with a fair degree of frequency and may be postcoital, menorrhagic, or

TABLE IX. PARITY OF 138 PATIENTS WITH BENIGN VASCULAR TUMORS OF THE UTERUS

PARITY	HEMANGIOMA			ANGIOMYOMA	LYMPHANGIOMA	LYMPHANGIOCYSTIC FIBROMA	TOTAL
	UTERUS	CERVIX	PELVIC SUPPORTING STRUCTURES				
Nullipara	8	2	1	9	1	3	24
Unipara or more	21	8	2	9	0	14	54
Not stated	13	7	1	28	2	9	60
Total	42	17	4	46	3	26	138

menopausal. Occasionally it may be severe enough to produce shock,[22, 28] and, in the case of intramural tumors, the cause of the bleeding is obscure. Bleeding associated with a large, diffuse vascular tumor may be the result either of increased vascularity of the uterus or of rupture of overdistended cavernous blood vessels, which have communicated with the endometrial cavity. Hemorrhage in the presence of submucous tumors is more readily understood.

Postcoital bleeding is most commonly noted with hemangioma of the cervix, and the most frequent diagnosis made, understandably, is carcinoma. The port-wine appearance of the new growth, however, is very typical of hemangioma, and blanching is readily produced by pressure, with return of the port-wine color when the pressure is released.

These uterine tumors are usually slow growing and rarely painful. Pain, when present, is the result of either increased pelvic congestion or degeneration within the neoplasm, most common with angiomyoma and lymphangiocystic fibroma. Rarely, however, growth of a hemangioma may be so rapid that pregnancy tests may be required to rule out an early gestation.

TABLE X. PRESENTING SYMPTOMS IN 138 PATIENTS WITH BENIGN VASCULAR TUMORS OF THE UTERUS

SYMPTOMS	HEMANGIOMA			ANGIOMYOMA	LYMPHANGIOMA	LYMPHANGIOCYSTIC FIBROMA
	UTERUS	CERVIX	PELVIC SUPPORTING STRUCTURES			
Hypermenorrhea	21	9	1	*	0	13
Postcoital bleeding	0	9	0	*	0	0
Postmenopausal bleeding	2	0	0	*	0	0
Abdominal pain	4	1	2	*	1	11
Rapid growth	1	0	1	*	0	3
Asymptomatic	6	2	0	*	1	0
Not stated	11	5	1	*	1	7

*Symptoms of angiomyoma are similar to those of fibromyomas, depending upon location and size of the tumor.

Treatment

Although recognition of most vascular tumors takes place in the laboratory, occasionally a diagnosis may be made at laparotomy. Diffuse cavernous hemangiomas have a characteristically bluish hue, and the uterus is softened and pulsating, greatly resembling its condition in pregnancy. Angiomyomas have a distinctive "ripe tomato" color.

Angiomyomas can be readily enucleated, but occasionally troublesome hemorrhage may be encountered, requiring hysterectomy for its control. Similarly, curettage for diagnosis may result in severe bleeding, also necessitating hysterectomy for control, and for removal of the traumatized vascular neoplasm (Tables VII, XI).

At best, radiation therapy has only a temporary effect on hemangiomas. Almost always the neoplasm tends to recur after a variable interval, and hysterectomy eventually is performed.

TABLE XI. TREATMENT IN 138 CASES OF BENIGN VASCULAR TUMORS OF THE UTERUS

OPERATION	HEMANGIOMA			ANGIOMYOMA	LYMPHANGIOMA	LYMPHANGIOCYSTIC FIBROMA
	UTERUS	CERVIX	PELVIC SUPPORTING STRUCTURES			
Dilatation and curettage	4					
Biopsy or amputation		8				
Polypectomy		4				
Hysterectomy	29	5	2	33	2	26
Myomectomy				5		
Autopsy	4			1	1	
Not stated	8	2	2*	7		

*One death occurred during laparotomy from hemorrhage; another patient had the tumor excised 6 years before, with recurrence 2 years after present operation.

Comment

Whether hemangiomas are vascular tumors, in the true sense, or are hamartomas is still somewhat doubtful. Many pathologists believe these tumors are congenital, particularly when involving the skin, resulting from a vascular maldevelopment. Angiomas of the uterus, however, are true neoplasms and, unlike those of the skin which lack the capacity for independent growth, they may attain a large size within a relatively short time, simulating pregnancy. Many such cases have been recorded, usually in women beyond the fourth decade of life. If these tumors were congenital, symptoms would more likely arise during the early childbearing years, rather than in later years, especially with submucous neoplasms.

The infrequency of angiomas of the uterus suggests a lack of relationship to leiomyomas, infection, trauma, or circulatory disturbances in other tumors.

The age at which vascular tumors of the uterus have their onset cannot be determined, but from Table VIII it can be noted that they belong chiefly to the late reproductive period and the decade following.

Early investigators believed that angiomas occurred only in previously gravid women, and that, somehow, they were related to changes at the placental site.[5] This view is not tenable, since these tumors appear in nulligravidas as well as parous women (Table IX).

A diffuse cavernous hemangioma may be a predisposing factor in rupture of the uterus during pregnancy. Spontaneous rupture at term during labor has been reported in two instances,[11, 29] and perforation of the uterus during curettage for incomplete abortion was noted by Duparque[2] and Halban.[8]

Despite lack of a true capsule, almost all hemangiomas of the uterus are benign tumors, although the marked cellularity so often noted in lymphangiocystic fibromas suggests malignancy. Only two of 26 reported cases of the latter neoplasm ended fatally, one from an associated endothelioma,[94] and the other from postoperative metastasis of an unrelated spindle-cell sarcoma.[87]

Reports of so-called "benign metastasizing hemangiomas" have appeared in the literature. These may have been benign growths which arose simultaneously from several mesodermal centers. Stout reported one such case wherein the patient exhibited three independent hemangiomas of the genital system in the uterus, vulva, and broad ligament.[33] Another case involving the uterus, cervix, and liver was reported by Lee.[6] Some "mestastasizing hemangiomas" appear to be malignant hemangioendotheliomas from the histological description, and, although metastases are described, these cases run a benign clinical course.[96-98]

Except for occasional references in the foreign literature, benign blood-vessel neoplasms have received little attention from gynecologists and gynecologic pathologists. Too little is known regarding the incidence of these tumors and the various types. Thus, Novak[99] stated that tumors of lymph vessels are more common than those of blood vessels, but the data herein presented indicate the reverse to be true.

It is most likely that more careful study of pathologic material would demonstrate more cases of vascular tumors of the uterus. Special staining of many highly cellular "cystic fibroids" probably would reveal many to be lymphangiocystic fibromas, as occurred in one of the cases included in this report.

Summary

Benign and malignant vascular tumors of the uterus have been classified. To 128 previously reported cases of benign blood vessel tumors of the uterus are added 10 more cases.

Histogenetically, these neoplasms arise from primitive mesoderm or from budding endothelial outgrowths of previously formed capillaries. Hemangiomas have their origin in blood vessels, and lymphangiomas arise from lymph vessels. Associated smooth-muscle growth results in angiomyomas, and associated fibrous connective tissue growth in lymphangiocystic fibromas.

Benign vascular tumors may be differentiated from simple telangiectasia by the presence of both old and newly proliferated capillaries within the neoplasm.

Such symptoms as appear are secondary to the size and location of the tumor within the uterus. The neoplasms bear no relationship to parity, but age does have some influence. The incidence of vascular tumors of the uterus is highest in the late childbearing years and during the early menopausal years.

Treatment is surgical removal of the tumors.

We wish to express our appreciation to Drs. Arthur Purdy Stout, Arthur T. Hertig, Louis M. Hellman, and Samuel A. Wolfe for their kindness in reviewing the manuscript.

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VASCULAR TUMORS OF THE UTERUS

II. Malignant Vascular Tumors

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IN A REVIEW of the literature we found that most reported cases of malignant vascular tumors of the uterus were published before 1920, and, because of the multiplicity of names used, as well as a lack of correlation of isolated case reports, a great deal of confusion exists regarding them. New histogenetic concepts and diagnostic criteria have necessitated reclassification of all vascular tumors of the uterus.[11]

A comprehensive clinicopathologic study of vascular tumors of the uterus was undertaken in order to clarify this group of neoplasms. Benign vascular tumors were the subject of the preceding article, Part I of the review. This section on malignant vascular tumors is based on 10 cases: 7 of hemangiopericytoma, of which 4 were previously published,[12] and 3 of hemangioendothelioma, obtained from a review and reclassification of all cases previously diagnosed sarcoma* or hemangioendothelioma of the uterus.

Angiosarcoma is the generic term applied to a malignant vascular neoplasm and includes several varieties of new growth based upon the cells of origin. An angiosarcoma is defined as a highly vascular tumor derived from mesenchymal angiomatous elements, which reproduces blood and lymph channels varying in the degree of maturity, and which may be occult or apparent. Angiosarcomas must be distinguished from some highly anaplastic sarcomas wherein groups of tumor cells may be noted arranged around vascular channels, particularly in areas of necrosis. Such tumors are designated as vascular sarcoma, indicating the presence of a rich blood supply. In addition, differentiation must be made from other rapidly growing neoplasms which may also have a rich blood supply. This is especially true for mesenchymal tumors, which are derived from the same primitive tissue as blood vessels. Thus, increased blood vessels within a new growth do not necessarily indicate a vascular origin of the tumor; only the presence of vessels in various stages of development and maturity points to an angioblastic derivation.

Intervascular cells of angiosarcomas vary from spindle shaped to round or polygonal. Such variation is not unexpected in view of the wide variety

*Review of sarcomas of the uterus was made by Drs. S. A. Wolfe, M. Schiffer, and A. Mackles, to whom we are indebted for some of the material included in this report.

of cells derived from primitive mesenchyme, which may themselves reveal marked plasticity. Since the uterus itself is of mesodermal origin, it is not surprising that differentiation of angiosarcomas from other tumors of the uterus is often quite difficult.

A classification of vascular tumors of the uterus, both benign and malignant, is given in the preceding article, Part I.

TABLE I. CASES OF HEMANGIOENDOTHELIOMA OF THE UTERUS REPORTED SINCE 1920

AUTHOR AND YEAR	AGE	PARITY	SYMPTOMS		THERAPY		SITE		METASTASIS AT OPERATION	REMARKS
			HYPERMENORRHEA	PAIN	HYSTERECTOMY	X-RAY	SUBMUCOUS	INTRAMURAL		
Murphy (1923)	41	iii		+	+			+	+	Died fourth postoperative day
Singer (1924)	41	vii	+		+			+		Died tenth day; autopsy
Cetroni (1930)	44	0	+	+	+			+		No follow-up
Valtorta (1937)	45	0	+		+		+		+	Rapid growth. Untraced
Kevorkian (1940)	34	i	+		+		+			Alive 6 years postoperatively. recurrence in cervical stump, x-ray therapy
Stout (1943)	28	–	+	+	+	+	+		+	Died 14 months postoperatively. Autopsy: metastasis
Knoll (1947)	50	–		+		+	+		+	Died in 4 months. Rapid growth of tumor; exploratory laparotomy. Autopsy: metastasis
Cohen (1949)	47	iii	+		+		+			Alive 3 years postoperatively
Authors (1)	57	iv			+	+	+			Alive 5½ years. Postmenopausal bleeding
(2)	37	ii	+		+	+	+			Alive 5½ years. Myomectomy
(3)	50	i		+	+					Alive 5 months. Subserous tumor

Morphology

Hemangioendothelioma.—This neoplasm does not have any gross characteristic features. The vascular nature of the tumor, however, is apparent from its red-to-purple appearance, although it occasionally may appear to be gray white, due to an absence of red cells in the blood vessels. The tumor is generally soft and friable, exhibiting vascular spaces of varying size and shape on cut section. In some areas proliferating endothelial cells may be seen to fill completely the lumina of the vessels. The delicate reticular framework of these spaces and the intraluminal growth of neoplastic cells are clearly revealed by silver reticulum stain, which also demonstrates an occult vascularity of the more solid portions of the neoplasm, and characteristic capillary anastomoses not apparent in hematoxylin and eosin preparations are now outlined. Stromal cells consist of elongated and polygonal cells which have grown outside the vascular sheath. These are arranged in cords or solid sheets, a pattern usually reproduced in metastases (Figs. 1-6).

Hemangiopericytoma.—While hemangiopericytoma has no distinguishing features, unlike hemangioendothelioma, its usual color is gray white to yellow in spite of its vascular origin. Absence of cyanotic-red coloration, so often noted in vascular tumors, is due to the presence of numerous noncanalized

proliferating capillaries within the neoplasm, as well as an absence of red blood cells within patent vessels. Occasionally, red cells are present, so that the tumor does have a red coloration.

Hemangiopericytomas vary in size from microscopic to 20 cm. or more. The smallest tumor of this series was 5 cm. and the largest 12 cm. Four uterine tumors were submucous, two were intramural but encroaching upon the endometrial cavity, and one was subserous. Absence of a capsule explains the marked difficulty often encountered when enucleation of a tumor is attempted, and hemangiopericytoma is similar, in this respect, to leiomyosarcoma and adenomyoma (Fig. 7).

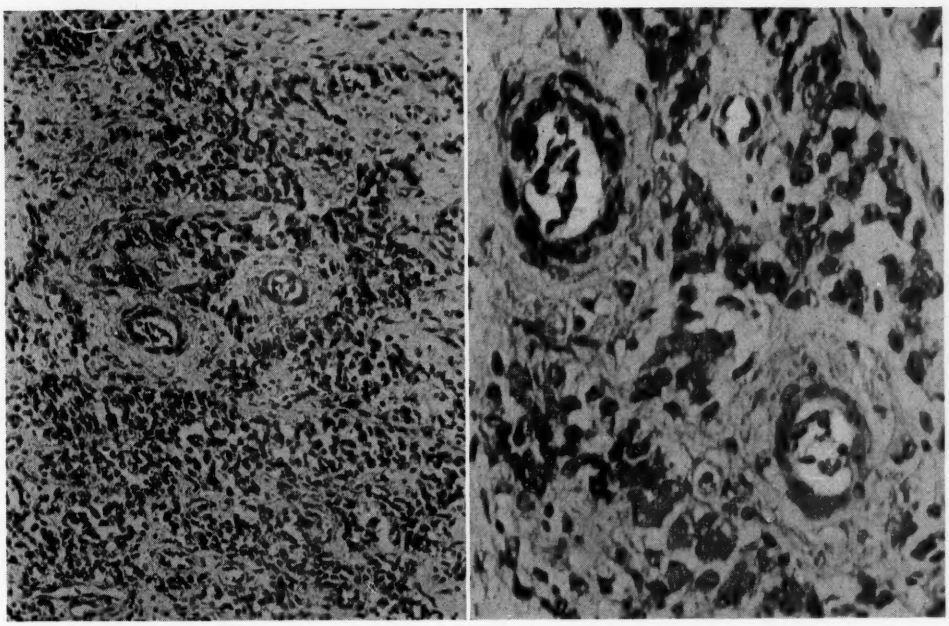


Fig. 1. Fig. 2.

Fig. 1.—S 47-4912. Hemanigoendothelioma. Numerous endothelial cells, with attempt at vessel formation. (Hematoxylin and eosin. ×150; reduced ⅕.)

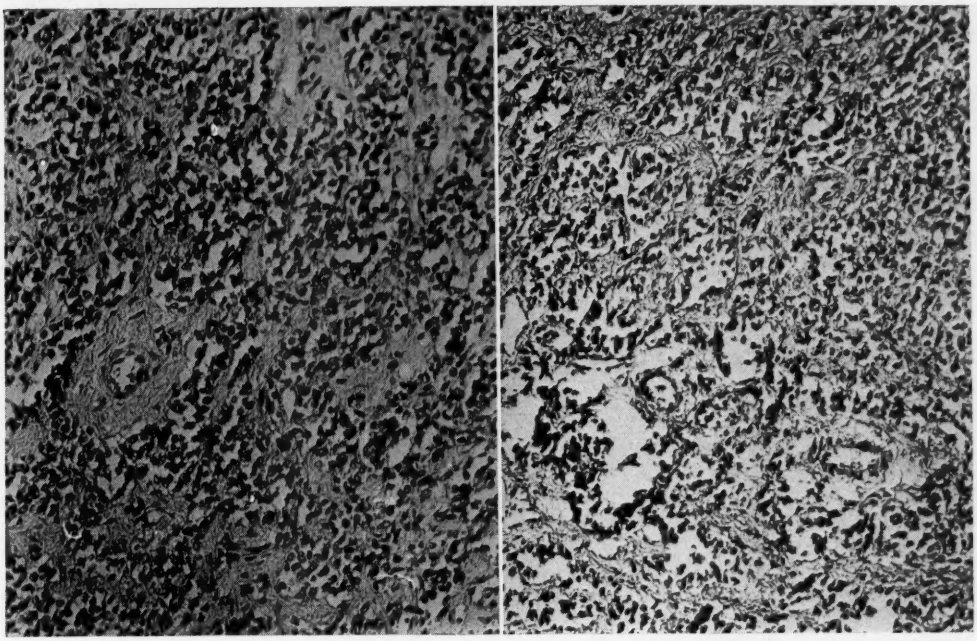
Fig. 2.—Same case. Higher magnification revealing "heaping-up" of endothelial cells in lumen of vessel. (Hematoxylin and eosin. ×440; reduced ⅕.)

Diagnosis is based on histologic examination of the tumor. Morphologic variations exhibited by pericytes account for frequently inconstant appearances so characteristic of hemangiopericytomas. The cells may be round, ovoid, or spindle shaped, and may contain a round or ovoid vesicular nucleus. Similarity of pericytes to smooth-muscle cells necessitates special differential stains, such as Masson's, to distinguish one type from the other. The cells of a hemangiopericytoma are concentrically arranged around the capillaries of the tumor (Fig. 8). Almost always proliferating capillaries may be noted on careful examination, although in some areas of the tumor these vessels may not be apparent when stained with ordinary hematoxylin and eosin. Silver staining demonstrates noncanalized capillaries, as well as those not apparent because of compression by an overabundance of pericytes. The vessel sheaths are stained black, so that the extraluminal position of the pericytes is emphasized (Figs. 9-12). In addition, connective-tissue septa may be noted enveloping both large and small aggregates of cells and, occasionally, isolated pericytes. The vascular sheaths often vary markedly in thickness, and the reticulum content of the neoplasm also shows considerable variability.

B.

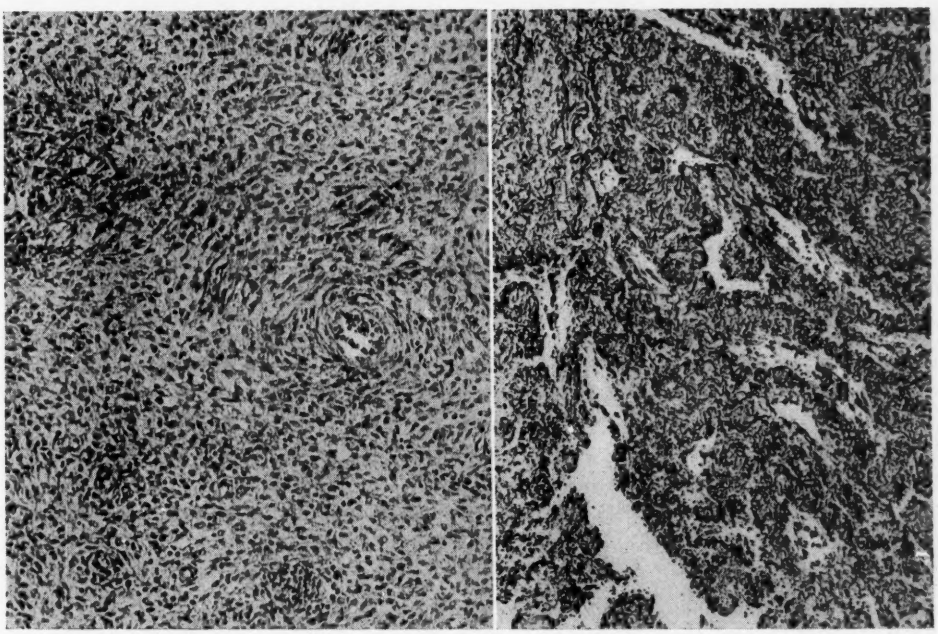
A.

Fig 3.—*A*, Same case. Silver stain to reveal numerous endothelial cells, with attempt at vessel formation. (Wilder's silver stain. ×150; reduced ⅕.)
***B*, Same case. Higher magnification, revealing "heaped-up" cells within vascular sheath. (Wilder's silver stain. ×440; reduced ⅕.)**



A. *B.*

Fig. 4.—*A*, Same case. Myometrium invaded by endothelial cells.
B, Same case. Silver stain revealing marked vascularity.

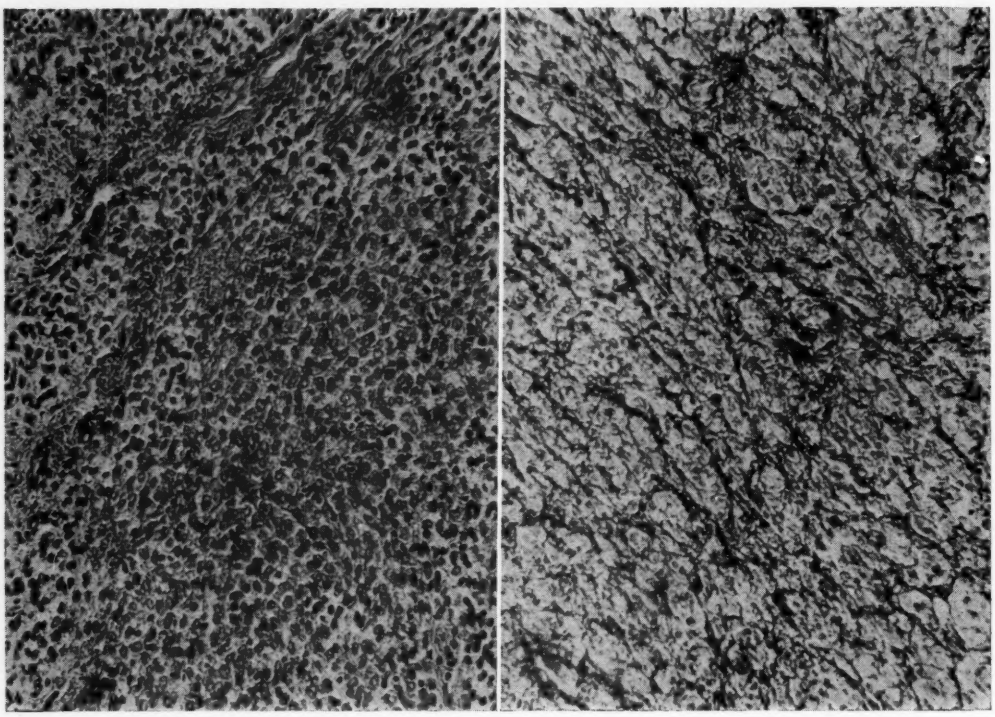


A. *B.*

Fig. 5.—*A*, S 48-429. Very cellular hemanigoendothelioma. (Hematoxylin and eosin. ×150; reduced ⅙.)
B, Same case. Silver stain to reveal marked vascularity.

Mitotic figures are rarely present, but when noted in large numbers signify rapid growth and possible future malignant course.

Occasionally nests of tumor cells may be observed lying free within lymphatic channels, but their significance in the absence of obvious metastasis is questionable (Fig. 13).



A. *B.*

Fig. 6.—*A*, S 53-2877. Hemangioendothelioma. (Hematoxylin and eosin. ×150; reduced ⅕.) *B*, Same case. (Wilder's silver stain. ×150; reduced ⅕.)

Kaposi's sarcoma is primarily a disease of the skin, more commonly found in males. No cases have been reported in which the uterus was involved.

Lymphangiosarcoma.—This tumor, also known as lymphangioendothelioma, is nonencapsulated and is composed of endothelial elements with a connective-tissue stroma. Budding endothelial elements give rise to lymphatics of varying size and shape, and the lining cells may proliferate either intro- or extraluminally. A highly cellular appearance of some areas of the neoplasm is usually the result of extraluminal proliferation. Except for occasional lymphocytes or clear fluid, the lymph channels are empty.

Lymphangiosarcoma bears a marked resemblance to hemangioendothelioma, except for absence of red cells within the vessels. Many hemangioendotheliomas, however, also may be devoid of red cells. Lymphangiosarcoma most frequently appears in areas where lymph stasis has occurred, such as postmastectomy lymphedema,[14] and therefore would not be expected to be present in the uterus; only two cases[9, 10] involving the uterus have been reported since 1920 (Table III).

Clinical Picture and Treatment

Malignant vascular tumors of the uterus most frequently affect women from the middle period of life through the sixth decade, with the greatest inci-

TABLE II. CLINICAL SUMMARY OF 7 CASES OF HEMANGIOPERICYTOMA OF THE UTERUS

CASE	AGE	PARITY	SITE		THERAPY		FOLLOW-UP AND REMARKS
			SUBMUCOUS	INTRAMURAL	MYOMECTOMY	HYSTERECTOMY	
No. 1							
First admission	25	0		+	+		Recurrence 6 months postoperatively
Second admission	28	0		+		+	Living 8 years postoperatively. Received x-ray therapy
No. 2	77	iii	+		+		Died 1½ years postoperatively. Had curettage 2 years and 3 years before vaginal myomectomy; hemangioma was not revealed. Postmenopausal bleeding not controlled by x-ray therapy
No. 3	71	i	+			+	Living 6 years postoperatively. Had radium insertion 2 years prior to hysterectomy for "endometrial polyps." Received postoperative x-ray
No. 4	43	i	+			+	Living 11 years. Tumor cells in lymphatics. Received postoperative x-ray therapy
No. 5	55	0				+	Died 1 year postoperatively. Menopause 8 years before. No metastasis at operation, but developed pleural metastasis after 7 months. Subserous
No. 6	42	iii		+		+	Living 6 months. Tumor cells in lymphatics
No. 7							
First admission	31	ii	+		+		Pathologic report, "fibroid." Readmitted 5 years later
Second admission	36	ii	+			+	

TABLE III. CASES OF LYMPHANGIOSARCOMA REPORTED SINCE 1920

AUTHOR AND YEAR	AGE	PARITY	SYMPTOMS		HYSTERECTOMY	SITE		REMARKS
			HYPERMENORRHEA	PAIN		SUBMUCOUS	INTRAMURAL	
Tuta (1942)	45	iv		+	+	+		Untraced
Limburg (1942)	35	i	+	+	+		+	Died several months postoperatively

dence in the fifth and sixth decades, similar to that of other malignant growths of the corpus uteri. Nulliparous, as well as multiparous, women may have angiosarcomas, and no special significance can be assigned to parity.

Metastasis is primarily via the blood stream, although spread of the growth may also occur by direct extension and through the lymphatics. Widespread metastasis is common.

Diagnosis of angiosarcoma is frequently not made until the removed tumor has been examined histologically. Enlargement of the abdomen may be the first sign noted by the patient. Bleeding, either as hypermenorrhea, polymenorrhea, or postmenopausal, is a common symptom; its presence is dependent upon the location of the neoplasm in the uterus in relation to the endometrial cavity. Abdominal pain results from degenerative changes or from rapid growth of the neoplasm.

Fig. 7.—Hemangiopericytoma. Gross section of uterus. Note lack of sharp line of demarcation between tumor and myometrium.

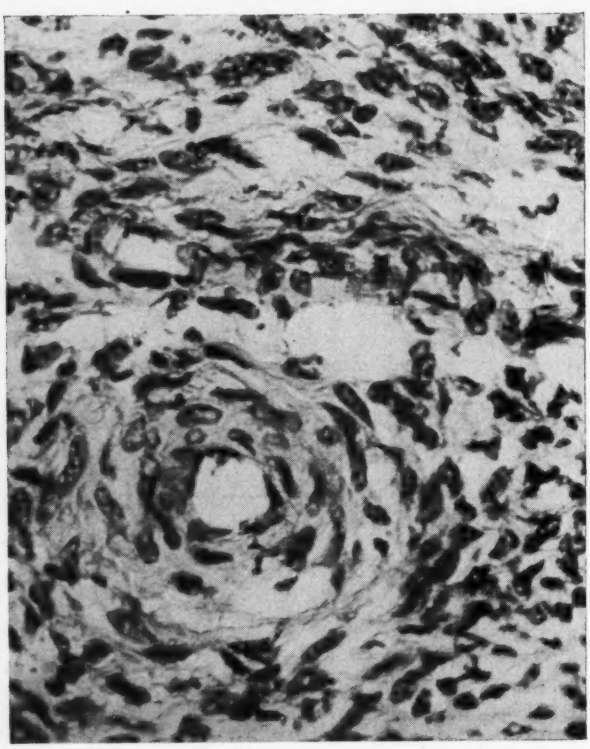


Fig. 8.—Hemangiopericytoma. Concentric arrangement of pericytes around capillaries. The "thick-walled" vessel is actually a capillary with condensation of pericytes and connective tissue. (Hematoxylin and eosin. ×440; reduced ⅕.)

Fig. 9.

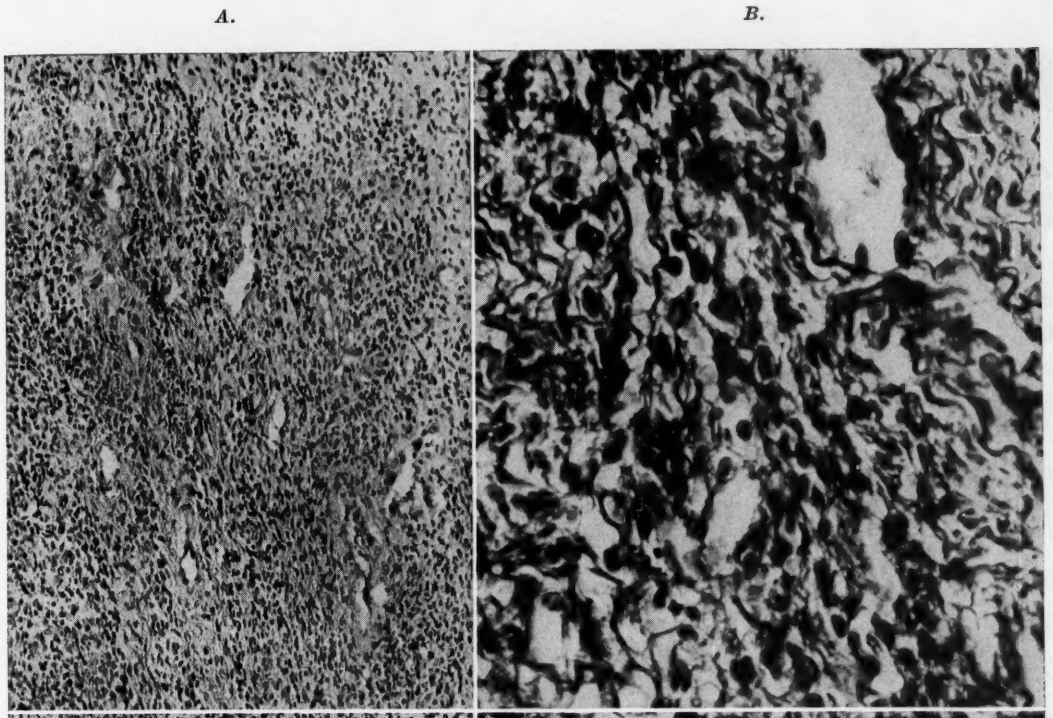


Fig. 10.

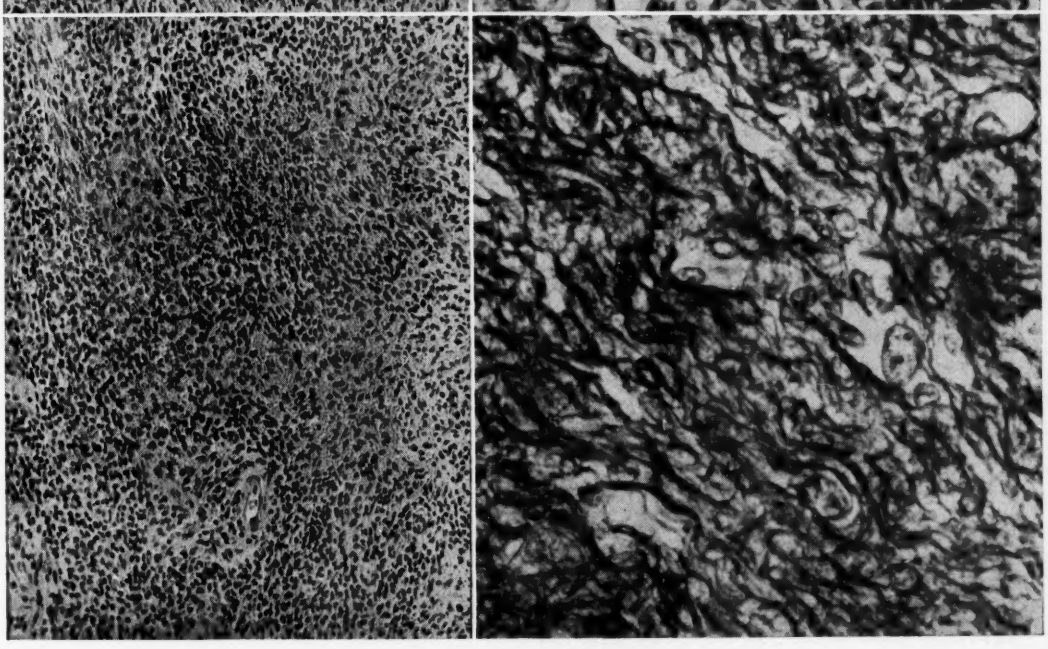
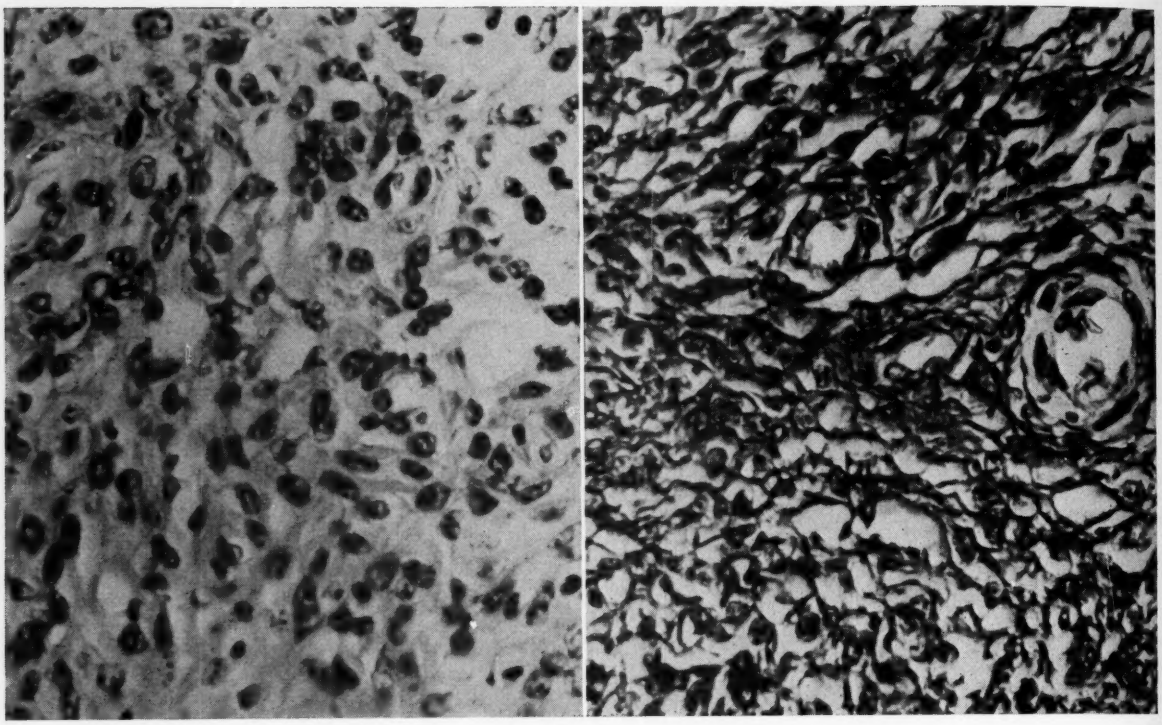


Fig. 9.—A, S 50-2979. Hemangiopericytoma (malignant). General appearance of tumor; obvious vascularity. (Hematoxylin and eosin. ×150; reduced ⅙.)

B, Same tumor stained with Wilder's silver stain. (×440; reduced ⅙.)

Fig. 10.—*A*, Same case. Another site from cellular portion of tumor. Vascularity not apparent. (Hematoxylin and eosin. ×150; reduced ⅙.)

B, Wilder's silver stain to reveal previously occult vessels. (×440; reduced ⅙.)



A. *B.*

Fig. 11.—*A*, Hemangiopericytoma (benign). (Hematoxylin and eosin. ×440; reduced ⅕.) *B*, Same case. Section stained with Wilder's silver stain. (×440; reduced ⅕.)

Whenever angiosarcoma is diagnosed, the preferred treatment is total hysterectomy with bilateral salpingo-oophorectomy, even when metastasis may be present. Since malignancy of hemangiopericytomas occurs in only 21 per cent of cases,[15] myomectomy may be performed, provided there is no evidence of metastasis, in order to preserve fertility. Total hysterectomy and bilateral salpingo-oophorectomy are indicated, if metastasis has occurred, to be followed by a course of deep x-ray therapy. Such irradiation should also be given postoperatively in all cases of hemangioendothelioma, although the value of postoperative x-ray for these tumors has not been conclusively demonstrated.

Prognosis

Hemangioendothelioma is far more malignant than hemangiopericytoma. Of the 11 cases of hemangioendothelioma reported since 1920, including 3 in the present paper (Table I and II), 4 patients (36.4 per cent) died within 14 months after operation; 2 could not be traced (although one may be presumed dead because of the presence of metastasis at operation); and 5 remaining patients were alive from five months to six years after operation. The five-year survival rate in the 11 cases of hemangioendothelioma was 27.3 per cent.

Since 1942, when hemangiopericytoma was first described by Stout and Murray,[16] only 13 cases of this tumor involving the uterus have been noted, including the first 4 cases herein listed.[12, 15, 17] Three additional cases are reported in this paper for the first time, making a total of 16 known cases of hemangiopericytoma of the uterus. Patients 2 and 5 died within one and one-half years after operation from metastasis, and on the basis of local recur-

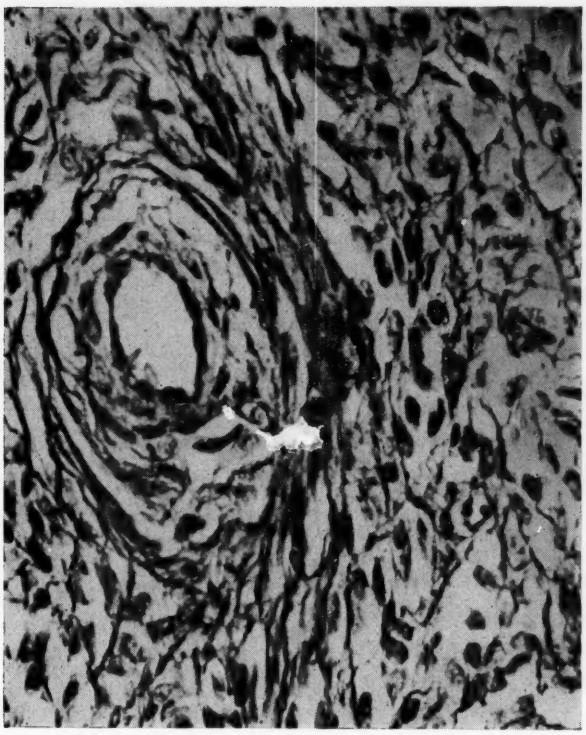


Fig. 12.—S 42-474. Hemangiopericytoma. Normal endometrial lining of capillaries. Note extraluminal position of pericytes. (Wilder's silver stain. ×440; reduced ⅕.)

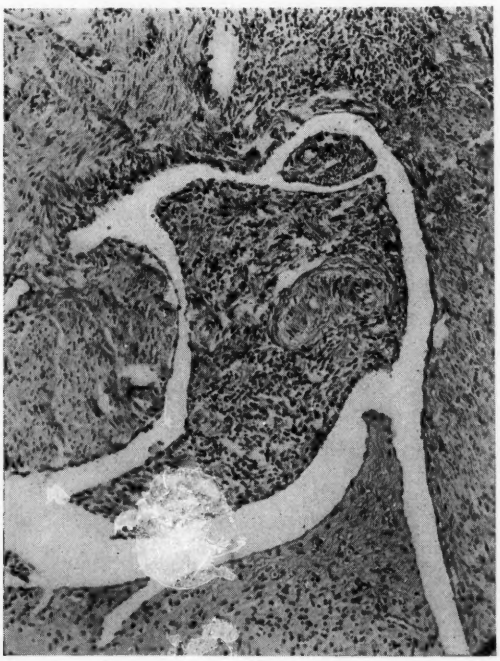


Fig. 13.—Same case. Nest of tumor cells lying free within a lymph channel.

rence of the tumor after excision, Cases 1 and 7 might also be considered malignant (Table II). Such recurrence may not actually indicate malignancy, however, for it may merely be a result of incomplete excision of the original neoplasm. These are the only known cases of malignant hemangiopericytoma of the uterus.

A total of 144 cases of hemangiopericytoma have been reported from various sites of the body, of which 21 per cent were malignant, based on either metastasis or local recurrence.

With recognition of more cases and a longer period of observation, better evaluation of the degree of malignancy of angiosarcoma will become possible.

Comment

A notable difference between hemangiopericytoma and hemangioendothelioma is the appearance of the endothelial lining of the vessels of each tumor (Figs. 3, 12). The endothelium of hemangioendothelioma exhibits marked proliferation within the vascular sheaths of the vessels, presenting a "heaped-up" appearance. The vessel wall itself is frequently invaded by the cells, with involvement of the adjacent extravascular tissue. Pericytes of hemangiopericytoma do not invade vascular sheaths, although free nests of tumor tissue may occasionally be noted within lymphatic channels. The endothelial lining of the blood vessels does not vary from normal.

From a review of the literature, it has become apparent that many reported vascular tumors will have to be reclassified. Most of those previously designated "perithelioma," and many designated "lymphangioendothelioma" more properly belong to the hemangiopericytoma group. Other vascular neoplasms belong to the hemangioendothelioma group. It has become evident that no definite conclusions in regard to malignancy can be obtained from the reported cases. As noted in a previous publication,[12] the malignant nature of hemangiopericytoma, in the absence of metastasis, can be determined only by subsequent clinical course of the disease. The usual histologic criteria of malignancy, however, are suggestive only of the future course and, although histologic evidence of malignancy was noted in 3 cases, these patients are still living eleven, five, and one-half years following removal of the tumors. There were 4 cases of hemangiopericytoma without microscopic evidence of malignancy; all had recurrence of the growth, and 2 patients have died.

The highly cellular appearance of hemangiopericytoma often creates confusion with sarcoma. The true nature of the tumor can be readily determined, however, by application of special reticulum and other connective-tissue stains. It is important to make this distinction, particularly in younger women, because so many hemangiopericytomas are benign and may be removed by simple excision of the tumor.

Relationship of Hemangiopericytoma and "Stromal Myosis".—Tumors that fulfill the criteria for hemangiopericytoma, as outlined by Stout and Murray,[16] have been diagnosed "endolymphatic stromal myosis,"[20, 21] "endometriosis interstitiale,"[22-24] "stromal endometriosis,"[25-28] "stromatous endometriosis,"[29] and "endometrial sarcoma."[30] Marked vascularity in all reported cases has been an outstanding characteristic, duplicated in recurrences

and metastases. In a case reported by Frank[20] a metastatic nodule which occurred 17 years after hysterectomy revealed an identical vascular pattern of the original new growth.

Another prominent feature of "stromal myosis" is the presence of thick-walled blood vessels which are thought to be arterioles. Hill,[31] however, has demonstrated that they are actually capillaries with condensation of surrounding connective-tissue fibers and stromal cells. Such vessels are also an outstanding feature of hemangiopericytoma. Many investigators believe that the blood supply of "stromal myosis" is derived from an ingrowth of endometrial vessels of the uterus. Severance of these vessels should, therefore, produce necrosis in the remaining tumor tissue, unless secondary vascular attachments have been established. Distant or late recurrence of the tumor following hysterectomy could not obtain its blood supply from the endometrium, and thus would not be expected to reproduce the original cytoarchitecture of the neoplasm, and particularly that of the blood vessels. This does occur, however, and suggests an origin of the tumor from vasoformative tissue, such as pericytes, rather than from mature stromal cells. While Embrey[29] and Hill[31] both believe that stromal cells are capable of forming blood vessels, there is no evidence that mature stromal cells can do so. All such neoplasms should be termed hemangiopericytoma, since similar tumors occur in other organs of the human body as well as the uterus. Hemangiopericytoma is generally benign, and it would be misleading to classify it as endometrial sarcoma rather than as a member of the angiosarcoma group of tumors. To do so would create a falsely grave prognosis for patients with a relatively benign neoplasm.

Summary and Conclusions

Review of uterine tumors previously classified as sarcoma and hemangioendothelioma has shown that 10 are vascular neoplasms: 3 hemangioendotheliomas and 7 hemangiopericytomas. Special stains are essential to delineate the basically vascular structure of angiosarcoma, as well as to distinguish various types of vascular tumors of the uterus.

Abnormal vaginal bleeding is the most common symptom associated with angiosarcoma. The preferred treatment for hemangioendothelioma and hemangiopericytoma with metastasis is total hysterectomy and bilateral salpingo-oophorectomy, followed by deep x-ray therapy.

Although hemangioendothelioma is very often malignant, hemangiopericytoma is relatively benign. A review of tumors previously designated "stromal myosis" revealed their appearance to be identical with hemangiopericytoma, a tumor found in other organs as well as the uterus. For that reason hemangiopericytoma, rather than "stromal myosis" or endothelial sarcoma, would better designate the new growth.

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9 PROSPECT PARK WEST (DR. PEDOWITZ)
524 NORTH AVENUE (DR. FELMUS)
555 PROSPECT PLACE (DR. GRAYZEL)

CARCINOMA OF BARTHOLIN GLAND. REVIEW OF THE LITERATURE AND REPORT OF A NEW CASE IN AN ELDERLY PATIENT TREATED BY RADICAL OPERATION*

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PRIMARY carcinoma of the Bartholin gland is a rare disease which has been reported with increasing frequency during the past ten years. As mentioned by Wharton and Everett,[40] this condition is probably much more common than is indicated by the literature, and it may be that many cases are not diagnosed as primary tumors or fail to be reported. In 1939, Simendinger[28] collected some 38 cases from the world's literature. Since that time there has been a total of 79 additional cases reported or more than twice the number found prior to 1939 in all the world's literature. This does not necessarily reflect an increase in carcinoma of the Bartholin gland but is probably due to more adequate diagnostic facilities being readily available to the medical profession and to the increasing tendency of physicians to report unusual and interesting diseases. The incidence given by Crossen[5] is 2 to 3 per cent of all vulval carcinomas which in turn comprise only 3 to 5 per cent of all female genital carcinomas. In other words, there is one case of Bartholin gland carcinoma to approximately every one thousand female genital cancers.

The reason for reporting an additional case is threefold: (1) to review the world's literature up to the present time; (2) to add to the literature an additional case; (3) to report a radical surgical procedure in an 83-year-old woman. As far as we can determine from reviewing the literature, this is the oldest patient to undergo and survive a radical vulvectomy with inguinal, femoral, and pelvic lymphadenectomy. A 91-year-old patient with Bartholin gland carcinoma was reported by Pape[21] in 1907. She underwent simple vulvectomy and resection of the inguinal glands, however. An interesting feature in the evaluation of our patient was a determination of her longevity. On reviewing the life expectancy charts of the Metropolitan Life Insurance Company, it was found that she had a calculated expectancy of five years and three months. If her life expectancy had been considerably shorter than this, a less radical approach to her disease might have been considered.

The first case to be reported was that of Klob[15] in 1864. During the following thirteen years a total of eight additional cases were added by Sinn,[29] Geist,[11] Schweizer,[27] and Mackenrodt.[19] In 1906, Chaboux[4] reviewed the literature and added one case. Thereafter Falls,[9] Schneider,[25] Simendinger,[28]

*Presented at a meeting of the Brooklyn Gynecological Society, March 17, 1954.

**American Cancer Society Clinical Fellow in Gynecology.

TABLE I. REPRESENTS AN ANALYSIS OF AQUINAGA'S AND THE PRESENT AUTHOR'S SERIES OF CASES OF CARCINOMA OF THE BARTHOLIN GLAND WITH A SUMMARY OF ALL CASES REPORTED TO DATE

SERIES	MEDIAN AGE	DURATION OF SYMPTOMS	TYPE OF LESION		TREATMENT		RESULT	
Aquinaga 1864-1944 77	49.8	9.5 months	(a) Epidermoid	31	(a) Local excision	32	Cured*	3
			(b) Adenocarcinoma	33	(b) Local excision plus radiation	15		
			(c) Sarcoma	3	(c) Radical excision with or without node removal	11	Died	15
			(d) Melanoma	1	(d) Radical excision with or without node removal, plus radiation	4	Unknown	56
			(e) Unknown	9	(e) Radiation alone	1		
Masterson and Goss 1944-1954 40	54.3	5.8 months	(a) Epidermoid	18	(a) Local excision	3	Cured*	7
			(b) Adenocarcinoma	19	(b) Local excision plus radiation	4		
			(c) Sarcoma	2	(c) Radical excision with or without node removal	10	Died	5
			(d) Melanoma	0	(d) Radical excision with or without node removal, plus radiation	2		
			(e) Unknown	1	(e) Radiation alone	1		
					(f) Other treatment or unknown	20	Unknown	28
Total 117	50.0	8.3 months	(a) Epidermoid	49	(a) Local excision	35	Cured*	10
			(b) Adenocarcinoma	52	(b) Local excision plus radiation	19		
			(c) Sarcoma	5	(c) Radical excision with or without node removal	21	Died	20
			(d) Melanoma	1	(d) Radical excision with or without node removal, plus radiation	6		
			(e) Unknown	10	(e) Radiation alone	2		
					(f) Other treatment or unknown	32	Unknown	84

*Indicates five-year survival.

Aquinaga,[2] LeDoux,[16] Crossen,[5] Wharton and Everett,[40] Abrams,[1] and Finn and McFadden[10] have added cases for a total of 116 cases to date. The addition of this case makes a total of 117. A comprehensive summary of the world's literature was made by Wharton and Everett[40] in 1951. The data given by these authors are not appreciably changed in the present report. Table I shows a summary of the cases collected from the literature by Aquinaga[2] in 1944. As mentioned by Wharton and Everett,[40] few authors have had an opportunity to observe more than a single case. The largest single series is that of Taussig[35] who included nine instances in 155 cases of carcinoma of the vulva. Reviewing the literature shows that many cases are listed in series of carcinomas of the vulva, and therefore no specific information can be obtained about the individual carcinomas of the Bartholin gland. For this reason many carcinomas of the Bartholin gland had previously been overlooked. Realizing this fact, Wharton and Everett were able to add 28 additional cases through careful search of the literature.

Carcinoma of the Bartholin gland occurs most commonly between the ages of 31 and 60 with the majority falling between the ages of 41 and 60 as noted in Table I. The youngest patient was an 18-year-old girl reported by Jarnecke,[14] the oldest being the previously mentioned 91-year-old patient. The median age is 50 years in this survey. This is nearly identical with the average age of 49.5 years reported by Wharton and Everett.

The symptoms associated with the onset of this tumor are nonspecific. The patient may complain of pruritus, abnormal bleeding, pain, or the presence of a tumor mass. Many of these patients have been treated for Bartholin gland abscesses and have undergone incision and drainage because of the central necrosis and inflammatory process associated with the malignant changes. Wharton, however, found that only 8.8 per cent gave a history of previous Bartholin gland infection. Hence, infection does not seem to be an important factor in the etiology of this carcinoma. No other factors seem to play a consistent role such as local lesions of the vulva, leukoplakia, and trauma.

Tabulating the types of tumor, Wharton found that 46.8 per cent were adenocarcinomas and 35.8 per cent were epidermoid carcinomas. However, in reviewing the literature to date (Table I), 107 of the carcinomas in which the microscopic diagnosis was available showed an incidence of adenocarcinoma of 48.6 per cent and epidermoid carcinoma of 45.8 per cent. There were also 5 sarcomas and one melanoma. In 10 cases the microscopic diagnosis was unknown. The number of epidermoid carcinomas appears to be surprisingly high considering that the tumor originates from a secreting glandular organ. Normally, squamous epithelium is found only at the duct orifice and transitional epithelium in the duct systems. However, Sitzenfrey[30] and Schweizer[27] have described squamous metaplasia occurring in the deeper portions of the gland during the course of chronic inflammation. Boughton[3] has repeatedly observed this phenomenon and feels that it probably explains the unexpectedly high incidence of epidermoid malignancy, especially when the tumor appears to arise in the deeper portions of the gland.

TABLE II. REPRESENTS ALL THE CASES THAT THE PRESENT AUTHORS HAVE COLLECTED FROM THE LITERATURE SINCE 1944 OR WHICH WERE NOT PREVIOUSLY INCLUDED IN AQUINAGA'S SERIES

AUTHOR	YEAR	AGE	DURATION OF SYMPTOMS	TREATMENT	TYPE OF TUMOR	RESULT
Schulz	1932				Epidermoid	
Eichenberg	1934	56	2 weeks	Removal with nodes. Radium and x-ray	Adenocarcinoma	Alive 4½ years
Wallis	1934	56	24 months	Excision	Fibrosarcoma	Alive 2 years
Taussig	1940				Adenocarcinoma Adenocarcinoma Adenocarcinoma Adenocarcinoma Adenocarcinoma Adenocarcinoma Epidermoid Epidermoid Epidermoid	Three five-year survivals reported
Cosbie	1940	64	1 month	Radical vulvectomy	Adenocarcinoma	Alive 3½ years
Smiley and Kushner	1942	44	1 month	Excision and x-ray	Myxosarcoma	Alive 2 years
Boynton	1943	54	6 months	Removal and x-ray*	Epidermoid	Died 6 years
Sperl	1943	45	24 months	Radical surgery and radium	Epidermoid	Died 3½ years
Hynes	1945	69	1½ months	Wide excision	Epidermoid	Alive 3½ years
Smith and Pollack	1947				Adenocarcinoma Adenocarcinoma	
Donnelly and Bauld	1948				Adenocarcinoma Adenocarcinoma	
Crossen	1948	64	1 month	Radical vulvectomy	Adenocarcinoma	Alive 3½ years
Curren and Healey	1949	37	12 months	Radical Surgery and groin dissection	Epidermoid	Alive 1 year
Leland	1949	57	12 months	Radical surgery*	Epidermoid	Alive 3 years

Lunin	1949				Combination therapy, no specific cases cited	Adenocarcinoma Adenocarcinoma Adenocarcinoma	
Sayre	1949	32	48	months	Excision and radiation*	Adenocarcinoma	Alive 23 years
Volpato	1950				Epidermoid		
Pattison and Shute	1951	41	3	months	Wide excision	Adenocarcinoma	
Watson and Counseller	1951					Adenocarcinoma Adenocarcinoma	
Wharton and Everett	1951	30	2	months	Unilateral excision and groin dissection with x-ray	Undecided	Died 13 months
		44			Radical local excisions, with or without groin dissections	Epidermoid	No five-year survivals—3 dead, one living
		74				Epidermoid	
		65				Epidermoid	
		37				Epidermoid	
Abrams	1952	54	17	months	Radical vulvectomy, cystectomy, inguinal and pelvic node dissection	Epidermoid(?)	Alive 18 months
Finn and McFadden	1954	55	1	month	Radical vulvectomy and groin dissection	Epidermoid	Alive 5 years
Masterson and Goss	1954	83	1	month	Radical vulvectomy and pelvic node dissection	Epidermoid	Alive 6 months

*Denotes that more than one course of therapy was necessary.

The diagnosis of this tumor may be difficult to make in its advanced stages because it may appear to be an extensive carcinoma of the vulva. In 1897, Honan[12] suggested 4 criteria for determining a primary Bartholin gland carcinoma. These have been fulfilled in the present case, as follows: (1) The site of the tumor is anatomically correct. (2) The tumor is deep in the labium. (3) The tumor has an intact overlying skin. (4) The tumor has some elements resembling glandular epithelium. There are cases reported which do not state whether or not all of these criteria have been met. They have led to some confusion in the past in gathering and reporting cases. It is therefore suggested that in the future these criteria be stressed and reported in subsequent clinical observations. The diagnosis then rests on a biopsy-proved malignant lesion which meets the conditions just given.

The treatment of primary carcinoma of the Bartholin gland has followed no accepted pattern, the number of cases having been too small to determine a regimen of therapy. In reviewing the literature it is obvious that all methods of therapy have been employed (Table I) including radium, x-ray, local excision, partial gland resection, and radical vulvectomy with a complete inguinal-pelvic lymphadenectomy. Various combinations of these procedures have been performed. Theoretically, the site of vulval carcinomas should offer an excellent opportunity for early diagnosis and therapy. Rabson and Meeker,[23] however, report that 15 months was the average interval between symptoms and the seeking of medical advice. In the present review, in 54 cases in which the duration of symptoms is known, the median duration of symptoms before consultation was 8.3 months. As with any carcinoma, this delay will result in a less favorable prognosis than would normally be expected. The vulva is a region which is readily accessible for inspection and biopsy by the physician.

Because of its anatomy it is also accessible to a surgical or radiological approach. This has been previously pointed out by Way.[39] It seems that the therapeutic approach to the disease should be identical with that in any carcinoma of the vulva, namely, surgical. Vulval tumors in the past have shown a poor response to radiation. Since the Bartholin gland is a vulval structure, the surgical approach should be attempted whenever feasible. The lymphatics of the vulva and vagina have been thoroughly investigated by Way and others. The lymphatic drainage from the lower portion of the vulva appears to be through the inguinal, femoral, and iliac chain of nodes. The deep femoral glands are probably among the first to be involved. For this reason it is suggested that a simple inguinal adenectomy is inadequate. The vaginal lymphatic drainage is probably into the iliac and hypogastric nodes. Experience in the past has shown that effective irradiation to this area is difficult to administer and the response poor. Therefore, the removal of all nodes appears to be the logical answer. Boughton[3] has previously shown that primary carcinoma of the Bartholin gland is a well-localized lesion with a surrounding capsule in its early stages and should have a better prognosis than the usual vulval carcinoma. It originates in a single site and not from a large area of leukoplakia (multicentric areas). Again, in reviewing the

literature, it is difficult to evaluate the end result since many individual combinations of methods have been employed. As will be mentioned later, many of these methods are inadequate.

In patients undergoing a two-stage procedure, the question of whether to do the vulva or groin dissection first has been debated by Way. It appears best to remove the tumor site first. In the present case, however, a rather severe fibrotic inflammatory reaction was found at the time of the second stage which made the inguinal gland dissection considerably more difficult from a technical standpoint. This might be a factor to take into consideration in the future whenever a two-stage procedure is contemplated. The groin dissection should, of course, be followed in a short interval of time by the second stage and removal of the primary growth. This might also have the additional advantage of allowing histological examination of the lymph gland and exploration of the pelvis. A more accurate idea of the actual stage of the disease would be obtained prior to subjecting the patient to a second radical surgical procedure.

The prognosis appears to be poor as indicated by a survival rate of less than 10 per cent in this survey. Finn and McFadden[10] have recently reported a five-year survival which brings the total number of patients to 10 who have survived this long or longer. In tabulating the survival rates, all patients with unknown survivals and those who were alive less than 5 years have been listed as "unknown." Of the 117 cases, there are 10 five-year survivors, 20 known to have died, and 87 unknown. The prognosis depends on the type of lesion, stage of development, size of the lesion and whether or not nodes are involved. Taussig, however, believes that the size of the lesion is more important than the gross involvement of the nodes. He found that with lesions of 4 cm. or less in diameter, the five-year survival rate was 52.6 per cent with node involvement and 63.6 per cent without node involvement. In lesions 4 cm. or more in diameter, however, the five-year survival rate was 50 per cent less in these same groups. These figures are for carcinoma of the vulva but because of the close analogy, it is felt that the same criteria might apply to Bartholin gland carcinoma. In general, then, the outlook should be favorable with this carcinoma if adequate therapy is instituted early. Table II lists the 40 cases reviewed during this study.

Case Report

Mrs. M. S. was an 83-year-old para iv-0-iv-i who was first seen at Kings County Hospital on Oct. 20, 1953, complaining of vaginal bleeding. The patient had an uneventful menopause 35 years prior to admission. She had had no unusual symptoms until five weeks prior to admission when she experienced three days of bright "vaginal" bleeding. At that time she discovered a tender tumor mass in the vulva. Past history was noncontributory except for a mild hypertension for the past five years, for which she had received no specific therapy. She had noted slight exertional dyspnea but no other signs or symptoms of cardiac decompensation.

Physical examination on admission showed a well-preserved Negro woman with a blood pressure of 200/90. General physical examination disclosed a mild cardiac hypertrophy. Examination of the perineum revealed a 3 by 2 cm. nontender, freely movable

mass in the right labium majus in the region of the right Bartholin gland. The stoma of the latter could not be identified. There was noted a superficial ulceration over the lesion and a punch biopsy was obtained. Pathological report on this specimen was "epidermoid carcinoma." The remainder of the pelvic examination showed a small, clean, atrophic cervix. The uterus was felt to be small, anterior, and freely movable. The adnexa were not palpable. There was no evidence of vaginal bleeding. Blood studies, chest x-ray, and electrocardiograph were all within normal limits.

Fig. 1.

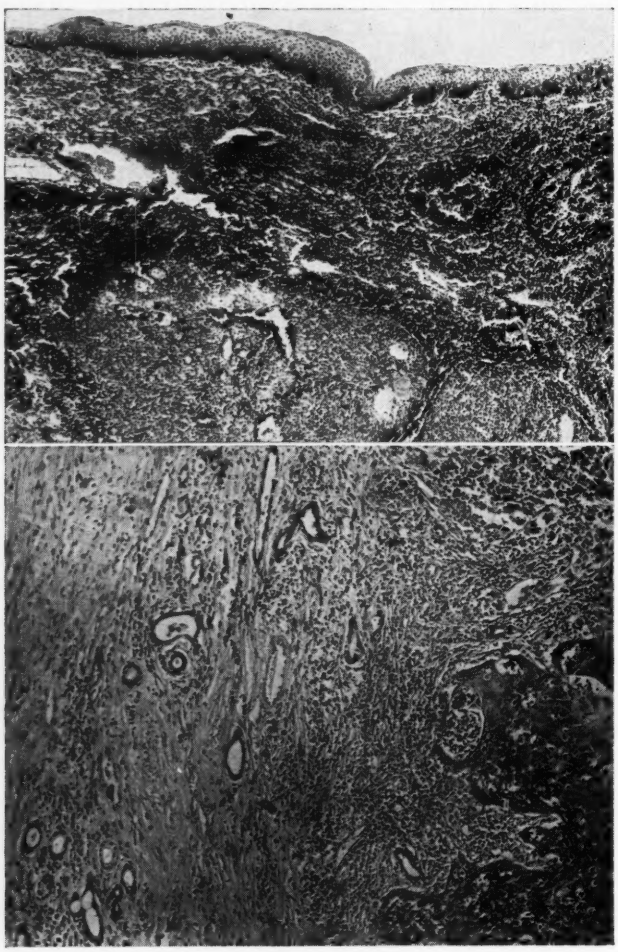

Fig. 2.

Fig. 1.—Section through edge of tumor showing intact surface epithelium. Marked inflammatory reaction of stroma. (Hematoxylin and eosin. ×60; reduced ⅕.)

Fig. 2.—Section showing normal Bartholin gland tissue infiltrated with epidermoid carcinoma. (Hematoxylin and eosin. ×150; reduced ⅕.)

On Oct. 30, 1953, under low spinal anesthesia, the patient underwent the first stage of a radical vulvectomy with wide removal of the vulva down to the pubic rami and approximately 4 cm. of vagina on the right side. After removing the specimen, it was examined and the lesion noted to be well circumscribed and giving no evidence of local extension. Microscopic sections above and below the lesion showed no extension beyond the confines of the Bartholin gland. The patient withstood the procedure well and was returned to the ward in good condition. Her postoperative course was uneventful.

On Nov. 18, 1953, she was again taken to the operating room and, under low spinal anesthesia, a bilateral inguinal, femoral, and pelvic lymphadenectomy was performed. There were many deep femoral nodes which were knotted and matted together. This resulted in considerable difficulty in dissecting these glands from the underlying vessels. A frozen section, obtained on one of these nodes during the operation, was reported negative for carcinoma. The incision was closed primarily, with drains inserted bilaterally in the medial angles of the wound, and the patient was returned to the ward in good condition.

The postoperative course again was uneventful and healing was per primam except for a small area over the region of the symphysis pubis. This area closed by granulation without further therapy. Two small local ulcerations developed in the inguinal wound that healed without specific treatment. The patient was discharged from the hospital on the thirty-second postoperative day. She has since been seen in the tumor follow-up clinic. At the time of her last visit on March 11, 1954, she appeared to be free of disease. There was a minimal amount of swelling in the right lower extremity.

Microscopic Description.—The surface of the specimen was covered by an intact layer of squamous epithelium. In the underlying fibrous connective stroma there were nests of glands of varying size lined by single layers of low columnar epithelium. The lumen of some of the glands contained mucus-like material. Intimately associated with these glands, there were columns and nests of polyhedral cells with hyperchromatic nuclei and abnormal mitoses. In some areas the cells showed marked disparity in size and shape with a tendency to epithelial "pearl formation" (Figs. 1 and 2).

Diagnosis.—Epidermoid carcinoma of the Bartholin gland.

Summary

1. An 83-year-old patient with primary carcinoma of the Bartholin gland has been presented. To our knowledge, she is the oldest reported patient to have undergone and survived a radical vulvectomy with inguinal and pelvic lymphadenectomy.

2. The world's literature containing 116 instances of carcinoma of the Bartholin gland has been reviewed and summarized.

3. The radical surgical approach to this lesion is recommended as the treatment of choice. It is felt that this tumor should be treated in the same way as other vulval carcinomas.

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TREATMENT OF FEMALE GENITAL TUBERCULOSIS*

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GENITAL tuberculosis in the female is almost always secondary to a tuberculous infection in another organ, usually the lung. It is generally agreed that the tubes are involved in practically all instances and that this involvement is bilateral in over 90 per cent of the cases.

When does infection of the tubes occur? Hematogenous seedings in the tube may occur when any tuberculous process in the body drains into the blood stream. This may be any time from several weeks to one year after the onset of the initial pulmonary infection. Auerbach[1] found such seedings in the presence of: (1) a primary complex in the lung; (2) an extrapulmonary tuberculous focus; and (3) a chronic pulmonary lesion. In 49 postmortem examinations in women with genital tuberculosis he found 10 cases of tubal involvement which occurred during the active stage of the primary complex when tubercle bacilli from the caseous lymph nodes drained into the blood stream. The primary complex and the hematogenous foci in other organs may heal while the process in the tube progresses. In 4 cases the tubal tuberculosis was associated with an active extrapulmonary focus (3 of tuberculosis of the vertebrae and 1 of tuberculous meningitis). Thirty-five cases occurred along with chronic pulmonary tuberculosis. In some cases, particularly those in the younger age group, the chronic pulmonary tuberculosis was of more recent origin than the tubal lesion, so that the tubal involvement developed from the primary complex. In most cases, however, the tuberculous process in the tubes was of shorter duration than that in the lungs and was a result of hematogenous dissemination from the lungs. The large majority of the patients with genital tuberculosis who come under the care of the gynecologist do not have active pulmonary tuberculosis. In many of these, the disease in the genital tract has been present for a sufficient period of time to allow for arrest of the pulmonary lesion.[2]

There are several factors peculiar to the anatomy and physiology of the female generative tract which present additional problems in the treatment of pelvic tuberculosis. The Fallopian tube, because of the numerous folds in its mucous membrane, offers an excellent nidus for further extension of the tuberculous process. Tubercle bacilli transmitted through the blood stream are deposited within the wall of the tube (usually in the submucosa) where they form tubercles. The caseous focus in the center of the tubercle, as it progresses, either involves the overlying mucous membrane or causes a pressure atrophy of the mucosa. After liquefaction, the caseous foci pour their bacilli into the lumen of the tube and may form an ulcer. At this stage adhesions

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of individual folds of mucous membrane may result in the formation of large cyst spaces, the so-called "pseudofollicular salpingitis." As a rule, however, the tubercle bacilli poured into the lumen of the tube stimulate the production of an exudate which bathes the mucous membrane and causes progressive caseation of the wall toward the serosa. It appears that the caseous extension occurs at a more rapid rate in the Fallopian tubes than in other viscera.[3]

About 90 per cent of the patients with pelvic tuberculosis are between 20 and 40 years of age. Since a large number of these patients are seeking help because of infertility, the desire to preserve the childbearing function tends to influence the treatment despite the fact that the possibility of full-term pregnancy ensuing after the onset of pelvic tuberculosis is extremely remote. Some maintain, however, that menstruation is essential for the well-being of a woman and at least this function must be preserved.

Because of the regularity with which the endometrium is shed at menstruation, tuberculosis affects the uterus differently than it does other organs, and the advanced stages—caseation, fibrosis, and calcification—are rarely seen during the reproductive period. The absence of caseation creates the impression that the lesions in the uterus are less serious than those elsewhere in the body. Such reasoning is dangerous and we would like to emphasize that active genital tuberculosis is a serious condition that may prove fatal even in the unsuspected case.

Classification

We are well aware that the specific treatment for each patient with tuberculosis must be individualized and that such variable factors as the activity, duration, type, and extent of the pelvic or extrapelvic disease, as well as the patient's allergy, resistance, age, nutrition, etc., govern the prognosis. For the purpose of this presentation, however, we shall consider two types of pelvic lesions, advanced and minimal.

In advanced disease endometrial tuberculosis is present, as well as palpable masses in the adnexa which are presumed to be tuberculous. Minimal disease is tuberculosis discovered in the endometrium by bacteriologic or microscopic methods. It is symptomless and there is no apparent evidence of tuberculosis elsewhere in the genital tract.

This classification is based on clinical evaluation of the extent of tubal involvement, since it is on the basis of this evidence that the type of treatment is determined. Recognition of the advanced types of pelvic tuberculosis presents little difficulty if the condition is borne in mind in the differential diagnosis of pelvic inflammatory disease. There undoubtedly is an intermediate stage between the advanced and minimal types of pelvic tuberculosis but this is not apparent on clinical examination. The minimal type of disease has also been described as unsuspected or latent pelvic tuberculosis.

Dosages of Antituberculosis Drugs

The antituberculosis drugs most frequently used today are streptomycin or dihydrostreptomycin, the isonicotinic acid hydrazides (isoniazid), and para-aminosalicylic acid (PAS). The dosages now recommended are:

1. Streptomycin or dihydrostreptomycin, 1 Gm. daily intramuscularly twice a week.

2. Isoniazid, 5 mg. per kilogram of body weight daily, orally in three doses (usually 300 mg. per day).

3. Para-aminosalicylic acid (PAS), 12 Gm. daily, orally in four divided doses.

The two most potent drugs in the treatment of tuberculosis are streptomycin and isoniazid. Some phthisiologists do not advise their combined use as the initial therapy for tuberculosis since it entails the risk of bacterial resistance to the two most effective antituberculosis drugs now available. Furthermore, it has not yet been determined whether the combination of these two major agents has a distinct advantage over the combination of a major agent and a minor agent (PAS). It is no doubt incorrect to attempt to fix a single streptomycin-PAS or isoniazid-PAS regimen that will be suitable for all cases.

Several factors influence the use of streptomycin or dihydrostreptomycin although both drugs may produce the same type of neurotoxic reaction.[4] In equal dosages streptomycin is less likely to cause deafness than is dihydrostreptomycin. Deafness is usually encountered after three or four months of therapy when the drugs are administered daily. Dihydrostreptomycin is less likely to cause vestibular dysfunction than is streptomycin when used in equal doses. If therapy for a prolonged period is contemplated, equal mixtures of streptomycin and dihydrostreptomycin may be employed. From the evidence now available it appears that bacterial sensitivity to streptomycin or dihydrostreptomycin is as well maintained on a twice weekly as on a daily regimen. These facts plus the use of PAS in combination with streptomycin have permitted the almost unlimited prolongation of streptomycin therapy without the occurrence of toxic reaction or drug resistance.

Isoniazid is as effective an antituberculosis agent as streptomycin and has the added advantage of ease of administration. The combination of isoniazid-PAS has gained widespread acceptance because both drugs can be taken orally and intramuscular injections over a long period of time can be avoided. The commonest toxic reaction to isoniazid is peripheral neuritis which is manifest by hyperesthesia of the feet and twitching of muscles. It is often possible to alleviate this condition by discontinuing the isoniazid and giving the patient large doses of pyridoxine hydrochloride (150 to 200 mg. daily). When the patient has been free of symptoms for several weeks, the isoniazid can be restarted. Other less frequent reactions to isoniazid are restlessness, insomnia, difficulty in initiating micturiton, variations in sexual stimulation, vertigo, and headache. These symptoms disappear when the drug is withdrawn.

Para-aminosalicylic acid is an extremely weak antituberculosis drug which finds its greatest usefulness in combination with a major agent. The dose of 12 Gm. per day is the largest dose tolerated by the average patient and must be altered to suit individual needs. The most common reaction to PAS is gastrointestinal disturbances (nausea, vomiting, and diarrhea) which may be so disturbing as to necessitate discontinuance of the drug. PAS may also produce such symptoms as skin eruptions, fever, and urticaria. It may also produce a thrombocytopenia which is thought to result occasionally in excessive bleeding at the time of operation.[5] We advise that it be discontinued for the week before operation and that small doses of vitamin K be given during this period.

Effect of Antituberculosis Drugs on Pelvic Tuberculosis

In the patient with advanced pelvic tuberculosis, the antituberculosis drugs may be expected to reduce the amount of inflammatory reaction by de-

creasing the activity of the infection in areas other than those that are caseous and to clear up ascitic fluid to a great extent when it is present. Operative procedures are rendered simpler by the separation of the pelvic organs from bladder, bowel, and omentum and by the partial resorption of the tuboovarian masses. Thus the dangers formerly inherent to surgery in the patient with pelvic tuberculosis, such as perforation of the intestine or bladder with resulting peritonitis from secondary infection or fistula formation, are greatly reduced. The caseous components of the disease remain, however. Marked hyperemia may be seen in the pelvis at the time of operation and bleeding may be more excessive than in laparotomy in the nontuberculous patient. This may be due to the effect of para-aminosalicylic acid as previously mentioned.

Mode of Action of Antituberculosis Drugs

In spite of the progress that has been made in the treatment of tuberculosis, there is at present no reason to believe that any drug or combination of drugs is sufficiently potent that other forms of treatment, such as rest, collapse therapy, or excision, may be disregarded. This is as true in advanced pelvic tuberculosis as it is in advanced pulmonary tuberculosis. Florey[6] believes that the response to treatment with antibiotics is dependent on the cytological pattern of the tubercle and the extent of caseation of the lesion. He has shown that in tuberculosis the chemical therapeutic agent must be able to penetrate the avascular caseous area surrounding the lesion, the wall of the giant cell, and the outer envelope of the tubercle bacillus. Streptomycin is effective directly in proportion to the blood supply of the lesion and has only a very limited action within the cell. PAS has no intracellular action. Isoniazid or its metabolites, because of the smallness of its molecule, is able to diffuse into caseous lesions.[7] In the presence of frank caseation in a tuberculous lesion of even moderate extent, however, none of the chemotherapeutic agents has been found to sterilize the infected area. On the contrary, careful culture techniques have shown that specimens removed surgically after an extensive course of therapy may still contain viable tubercle bacilli. What is accomplished is that the exudative components of the lesion are temporarily controlled so that no further spread occurs or perhaps some regression takes place during the period of chemotherapy. It is during this period that surgery should be performed.

Treatment

Duration of Preoperative and Postoperative Treatment.—

Our understanding of the mode of action, effectiveness, and optimum duration of therapy of the present group of antituberculosis drugs is based, for the most part, on the results of their use in a large group of patients with pulmonary tuberculosis. The rapid clearing of x-ray shadows during the first three months of therapy represents the resolution of nonnecrotic lesions in the lungs and by analogy the same effect may be presumed to occur in advanced pelvic tuberculosis.

In the treatment of pulmonary tuberculosis, the so-called "target point" is reached when: (1) the lesions become stable; (2) the cavities are closed; and (3) tubercule bacilli are eliminated from the sputum.[22] Termination of chemotherapy before the target point often results in relapse. While definite time limits cannot be set for the duration of chemotherapy in the individual patient, our experience has been that in the patient with advanced pelvic tuberculosis the maximum effects are generally reached within three months. The antituberculosis drugs are continued for a period of at least nine to twelve months postoperatively to control any spill or spread of infection at the time of operation and to arrest any small foci of tuberculosis that were not or could not be removed at operation.

Treatment of Advanced Genital Tuberculosis.—

After the diagnosis has been confirmed, the patient with advanced pelvic tuberculosis is given a course of the antituberculosis drugs for 90 to 120 days and pelvic examination is recorded by the same observer at least every 2 weeks. Usually the adnexal masses will become smaller and more discrete for a period up to 60 days, following which no further change occurs. For several days before operation the patient is given either penicillin or Terramycin and these drugs are continued for three to five days postoperatively. Regardless of age, a total hysterectomy and bilateral salpingo-oophorectomy are performed.

In a patient 40 years of age or older, such surgery would not be considered radical. The same procedure performed for similar disease in a woman in her early twenties might be criticized, however. For those who would question the "radical" procedure in the younger age group, we offer the following explanation. In the patient with advanced pelvic tuberculosis the disease has undoubtedly been present for a sufficient period of time for necrosis or caseation of tissues to have occurred. We have no way of knowing whether such changes have occurred in a uterus that is not removed despite the fact that repeated biopsy or curettage is negative. While we are in accord with the principles of preserving healthy organs, we believe that conservatism may be misplaced when there is a possibility that the organ is diseased. Tuberculous endometritis has been shown to persist after removal of the tubes and its cure by curettage is remote.[2, 8, 9] It is conceded that the tube is the main source of reinfection of the uterus, but it is not the only one, and reinfection may occur from the myometrium, from tuberculous foci in the basal layer of the endometrium, or from infected blood and mucus at menstruation. Bacteriologic studies of removed portions of lung in patients treated over a year with streptomycin and PAS have shown viable tubercle bacilli. In other extrapulmonary foci, the ineffectiveness of the antituberculosis drugs in caseous lesions has been proved by examination of the surgically removed organs.

We believe, therefore, that in advanced pelvic tuberculosis in which tubo-ovarian masses are present at the time of operation, the procedure that offers the patient the best chance of permanent cure is total hysterectomy and bilateral salpingo-oophorectomy. Failure to remove foci in the pelvis has resulted in a reactivation of tuberculosis in other parts of the body at a later date. Following operation the antituberculosis drugs (a combination of isoniazid or streptomycin with PAS or Terramycin, or streptomycin and isoniazid) should be continued for nine to twelve months or longer.

Treatment of Minimal Pelvic Tuberculosis.—

We have defined minimal pelvic tuberculosis as that discovered by bacteriologic or microscopic examination of uterine tissue or secretions. No palpable disease is present on satisfactory pelvic examination and the assumption is that there is also minimal involvement of the tubes although this cannot be ascertained with certainty except by microscopic examination of serial sections of the tubes. Basing the therapy on the reasoning that endometrial tuberculosis in the menstruating woman differs from that in other parts of the body because the frequent shedding does not allow sufficient time for the formation of large caseous foci, several investigators[10-13, 21] have attempted to eradicate endometrial tuberculosis completely by the use of chemotherapy. This has usually consisted of a course of chemotherapy for 90 to 120 days followed by repeated biopsy or curettage approximately every three months. It should be mentioned here that a negative curettage is much more significant than a negative biopsy since more tissue is available for examination in the former procedure. Furthermore, culture or guinea pig inoculation of endometrial tissue or menstrual secretions has given positive results when microscopic examination was negative. If both bacterio-

logic and microscopic examinations, repeated at regular intervals, remain negative, and if no untoward signs or symptoms appear, the patient is kept under careful observation without further therapy. Thus far reports have indicated recurrences of tubercles in the endometrium in over 10 per cent of patients followed for two years, even in those with a favorable early response.[10, 11, 21]

There are several unanswered problems in the chemotherapy of minimal pelvic tuberculosis that will require years for proper evaluation. Surgical removal of tubes healed by antibiotic therapy may reveal them to be so disorganized as to render them functionless, as stated by Ekengren and Ryden.[14] The occurrence of intrauterine pregnancy with delivery at term has been extremely rare with the previously described regimen of chemotherapy after positive diagnosis of tuberculous endometritis has been made.

Even if the minimal endometrial lesions are actually of recent origin, and may therefore be expected to react most favorably to the antituberculosis drugs, the lesions in the tubes are undoubtedly older and more advanced and may therefore contain necrotic or caseous components not amenable to drug therapy. As a matter of fact, there are some[19, 20] who state that the tubal tuberculosis persists after the eradication of the endometrial lesion and advise that the tubes be removed in patients with genital tuberculosis as soon as the diagnosis is established.

It is possible that antimicrobial therapy for three to four months is too short a time to obtain maximum results. More favorable results have been obtained in the treatment of minimal pulmonary lesions when antituberculosis drugs were continued uninterruptedly for nine to twelve months than when they were used for shorter periods. In order to determine the results of longer periods of antimicrobial therapy in minimal pelvic tuberculosis we are suggesting the following regimen: The patient should be given a course of streptomycin and isoniazid as follows: 1 Gm. of streptomycin twice weekly, intramuscularly, for a period of three months; isoniazid, 5 mg. per kilogram daily, orally (usually 300 mg. per day), to be started with the streptomycin and continued for one year. Four months after cessation of treatment, bacteriologic and microscopic examination of endometrial curettings and secretions should be done. If these are negative, a Rubin test or uterosalpingogram may be done the following month. If tubal patency is evident some hope for conception exists, although mere patency is not proof of tubal function that would enable passage of a fertilized ovum.[15]

Bacteriologic and microscopic studies should be repeated in these patients every four to six months for a period of several years. If recurrence is noted at any time, the patient should receive a course of streptomycin and isoniazid for three months and then be subjected to operation. The question arises whether this regimen and constant surveillance are worth while. For the young patient who is desirous of becoming pregnant and who will cooperate in her treatment, it probably is. When a sufficient number of patients treated by this method have been followed for five to ten years, a more definite answer can be given as to the number of pregnancies that have occurred.

We wish to emphasize that this prolonged regimen of chemotherapy which we have suggested is not a laissez-faire attitude. We are not in agreement with those who state that since minimal or unsuspected tuberculosis is discovered in symptomless women in apparent good health there is no reason to subject them to treatment, particularly surgery.[16] This would be a dangerous policy to adopt in so insidious and treacherous a disease as tuberculosis, and fatal cases of miliary tuberculosis have been reported when it was followed.[2, 11, 17] The danger of miliary or meningeal tuberculosis is extremely remote, however, in a patient receiving isoniazid. Dr. Walsh McDermott of the New York Hospital

states he has never encountered this complication even in patients with advanced cavitary disease in the lungs on isoniazid therapy. We have not suggested PAS in this regimen because it frequently leads to such severe genitointestinal symptoms that it must be discontinued after several months. Streptomycin is given for only three months because its maximum effect is probably obtained in this period and because it has been our experience that ambulatory patients, especially those without symptoms, will not persist in the therapy for long periods. Furthermore, it is the opinion of Dr. McDermott that isoniazid alone is probably just as efficacious as the combination of streptomycin and isoniazid in this type of minimal lesion.

There are some who believe that the use of antimicrobial therapy will result in more conservative operative procedures for genital tuberculosis. The greatest difference of opinion exists as to whether the uterus and the ovaries should be removed in addition to the tubes. If recurrence of tuberculosis in the endometrium is noted after a course of chemotherapy, it would appear inadvisable to retain the uterus. If repeated microscopic and bacteriologic examination of uterine contents revealed no evidence of tuberculosis and if at operation only the tubes and not the ovaries were involved, and if all this occurred in a young patient who was desirous of retaining her menstrual function, conservative surgery might be attempted. Since disease within the ovary cannot be ascertained at operation unless the ovary is bisected, this procedure should be carried out before the decision to retain the ovaries is made. If both ovaries are removed, there would be no reason for leaving the uterus. Careful follow-up on such a patient would be imperative. Whether conservatism is warranted is a question that cannot be answered at present. I believe the problem should be discussed with the patient and the course of the disease explained before a decision is reached.

Treatment of Tuberculosis Diagnosed at Operation.—

Although the diagnosis of genital tuberculosis is now being made more frequently than heretofore, there will be occasions when the lesion is first discovered at the operating table. In the presence of extensive disease, a bilateral salpingo-oophorectomy and hysterectomy should be performed. If such a procedure cannot be carried out because of technical difficulties, the abdomen should be closed without drainage and a course of antituberculosis drugs given for 90 to 120 days. Repeated pelvic examinations will usually show such regression of the disease as to enable operative removal of the diseased organs at a later date. Postoperative chemotherapy should be given for nine to twelve months.

Treatment of Tuberculosis Diagnosed by Microscopic Examination Postoperatively.—

Occasionally the pathologic diagnosis of a pelvic organ removed at operation reveals unsuspected tuberculosis. If inadequate surgery, such as salpingostomy, unilateral salpingectomy, or subtotal hysterectomy has been performed, the patient should receive a course of antimicrobial therapy and should be reoperated upon. If all the diseased organs were removed at the original operation, then a course of antimicrobial therapy postoperatively is all that is necessary.

Treatment of Tuberculosis of the Cervix.—

Tuberculosis of the cervix is usually secondary to disease in the body of the uterus and the tubes. It has been reported in about 3 per cent of cases of genital tuberculosis although in a recent series it was found in 16 per cent of the patients.[18] Repeated microscopic and bacteriologic examinations, total, rather than subtotal, hysterectomy, and more careful examination of the cervix removed at operation were responsible for this higher incidence of tuberculous cervicitis. Treatment for tuberculosis of the cervix should be similar to that

for advanced pelvic tuberculosis, that is, radical. Sered has reported 9 cases of tuberculous cervicitis treated up to 120 days with antimicrobial therapy and in every case in which operation was performed, tuberculosis was present in the uterus or tubes at the time of operation.

Radium and X-ray in the Treatment of Genital Tuberculosis.—

Although radium or roentgen therapy has been used sporadically in the treatment of genital tuberculosis, the large majority of the investigators do not favor its use for the following reasons: (1) The focus of infection is not removed. (2) Roentgen rays may cause a breakdown in a tuberculous lesion and intrauterine radium may reactivate disease in the tube. (3) The ovaries are destroyed. (4) If the results attributed to pelvic irradiation in tuberculosis, such as destruction of the tubercle bacillus or its surrounding lymphoid or epitheliod cells, or encapsulation of the disease by stimulation of connective tissue formation, etc., were true, it seems to me that it would have gained more widespread use in the treatment of tuberculosis in other parts of the body. This has not been the case.

Summary and Conclusions

Active pelvic tuberculosis is a serious disease and even the unsuspected "minimal" case may prove fatal. The prognosis is not determined entirely by the presence or absence of adnexal masses on palpation, for the probability of the tubes being involved in all cases of genital tuberculosis is very great. At the present time the treatment of advanced female genital tuberculosis should consist of the general measures used to treat tuberculosis elsewhere in the body, antimicrobial therapy pre- and postoperatively, and surgical excision of tuberculous tissue as determined in each individual case. We favor radical surgery, that is, total hysterectomy and bilateral salpingo-oophorectomy, in these cases. The increasing incidence of tuberculosis reported in the uterus when careful examinations are carried out even after long periods of chemotherapy, plus the fact that reactivation of tuberculosis is so common from what is considered healed or arrested foci, has lead us to this view. Furthermore, even if healing does occur, the tubes are so distorted that a normal pregnancy is extremely unlikely.

There are some who believe that antimicrobial therapy will enable one to perform more conservative procedures. Morbidity and mortality need no longer influence our decision as to whether to do radical or conservative surgery since the preoperative use of the antituberculosis drugs has greatly simplified the surgical procedures and has markedly reduced the operative and postoperative complications. The youth of the patient, plus the desire to retain the menstrual function, may sway the operator to conserve the uterus and ovaries. In such a case the patient must be kept under constant observation for several years since reactivation of tuberculosis in the pelvis or elsewhere in the body has been known to occur within 2 years of the cessation of treatment.

I have suggested a prolonged course of antimicrobial therapy for the patient with early minimal pelvic tuberculosis. Since such cases are not common in one hospital or in one gynecologist's practice, it might be advisable to set up a registry where results of this or other forms of treatment could be recorded, so that a large number of cases can be assessed. This will enable us

to determine, in a shorter period of time, whether a sufficient number of patients have successful intrauterine pregnancies to make this long regimen worth while.

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A SIMPLE SLING OPERATION FOR THE TREATMENT OF STRESS INCONTINENCE

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STRESS incontinence is a very distressing and oftentimes embarrassing symptom, most frequently associated with urethrocele, cystocele, and injuries to the bladder neck. Many operations have been devised since this entity first aroused interest among gynecologists, some being fairly simple procedures, such as those described by Kelly, Kennedy, and later modified by Te Linde, but many of the others, mostly abdominal in approach, or combined vaginal and abdominal operations, are formidable undertakings so that few gynecologists even attempt the suprapubic approach and the patient is left to believe the defect is beyond repair. Yet the mere fact that concepts have differed and continue to differ on how to cure the dribbling of urine can signify only that no single operation devised so far has proved to be the ultimate cure for this ailment. It is generally agreed that the vaginal approach should be the procedure of choice in rectifying stress incontinence and only a comparatively few fail to benefit by the operation. Every gynecologist has seen these unfortunate patients occasionally and debated the proper treatment to institute for their relief.

Heretofore, one was compelled to choose between a repeat vaginal plastic repair, or an array of so-called sling operations or vesicourethral suspensions in which ligaments, with their attached muscles, have been transplanted, or fascias of the body used to serve as a sling for the urethra. Basically, the mechanism of the sling placed below the urethra (1) narrows the urethral canal by pressure; (2) adds support to the urethra; (3) aids the voluntary contraction of the urethra when stimulated; (4) tightens the fascial planes about the urethra and bladder neck; and (5) restores the urethrovesical angle.

The scope of this paper does not permit a review of all the methods designed to correct recurrent stress incontinence after previous failures. Most of the sling operations in use today are based on the combined technique known as the Goebell-Frankenheim-Stoeckel operation, in which the pyramidalis muscles with a free end of rectus fascia attached are passed backward retropubically and sutured under the urethra, after a preliminary plication of the vesical neck by the vaginal route.

Few, if any, improvements were made in this operation until Miller modified the technique by placing the rectus fascial strips beneath the urethra, anterior to the symphysis pubis, thus eliminating the excessive bleeding encountered in bringing the fascial strips between the pubis and the bladder. Later,

Aldridge presented a new technique with the use of fascial strips from the aponeurosis of the external oblique, which passed through, instead of between, the rectus muscles. Still, somewhat later, Millin and Read described an operative technique with the use of the aponeurosis sling passed under the bladder neck and proximal urethra from above by means of a special instrument.

This describes briefly what I feel are the leading sling operations used in most clinics today. But heretofore the surgeon was fearful of these time-consuming procedures, and the vesicourethral suspension operation as described by Marshall and Marchetti, in which the fascia surrounding the urethra and bladder neck was sutured to the posterior portion of the symphysis, has become increasingly popular. Though it is not difficult to perform, in my hands, at least, it has not yielded the same gratifying results as the sling operation. In my meager experience, the sutures were sometimes difficult to place into the periosteum which frequently tore, and, when they did hold, the tension seemed to be unduly great, giving the impression that pressure necrosis frequently ensued with subsequent release of the suspension.

It seemed to me that the sling operations afforded a much greater degree of flexibility, but, because of their complexity, involved more operative work than was necessary. Most of the difficulty arose in placing the sling under the urethra. This was extremely hazardous when attempted from above because of the presence of scar tissue likely to be encountered from previous vaginal plastic operations, making it difficult to break through, and lacerations of the urethra oftentimes occurred as unpleasant complications. Also, for the inexperienced, it was frequently difficult to determine the exact tension of the straps and, if one became a bit overzealous, postoperative obstruction could occur from too tight straps. Therefore, if the technique could be simplified, it was felt that many more gynecologists would employ the operation and many more women would lead happier lives as a result.

It is not difficult to raise the straps of fascia from the rectus sheath for the sling, but since the placement of the straps beneath the urethra was the laborious and toilsome portion of the operation, it was decided to eliminate this step by simply sewing the fascial strips to the pubocervical fascia on each side of the urethra and bladder neck, the portion of the fascia beneath the urethra serving as a natural sling. In this manner, the tension of the straps would accomplish the same objectives necessary to effect a cure of the stress incontinence, without undermining the urethra; i.e., they would add support to the urethra, the urethra would be elongated and narrowed, and they would voluntarily contract the urethra when stimulated. Furthermore, there would be no possibility of overkinking the urethra by too tight straps, and it would be quite possible to plicate the lumen of the overstretched urethra and bladder neck in order to reduce the size prior to suturing the flaps.

By employing this technique, I have now done three cases with excellent results in all. Admittedly, the series is small, but the end results were so uniformly good that it was deemed advisable to publish this preliminary report.

CASE 1.—The patient was a 45-year-old para iv, who complained of a pain in the left side and dribbling of urine on coughing and sneezing. The essential physical findings were multiple fibromyomas and a large cystocele. A panhysterectomy, bilateral salpingo-oophorectomy with appendectomy was performed, following which the peritoneum was closed and the previously described strap operation carried out.

CASE 2.—The patient was a 26-year-old para iii, who stated that she had been suffering from a chronic backache during the past four years, this becoming almost continuous during the last several months. During each pregnancy, it was necessary for her to wear a pessary for three to four months, and after each delivery the backache seemed to grow worse. The patient also added that she had difficulty holding her water, especially on coughing or straining, and that she was wet practically all the time. Examination showed a retroverted uterus and a moderate-sized urethrocele but no cystocele. Manual replacement of the uterus, with the wearing of a pessary, provided complete relief of the backache. A modified Gilliam hysteropexy and appendectomy was done and after the peritoneum was closed the bladder neck suspension was carried out by the aforementioned technique.

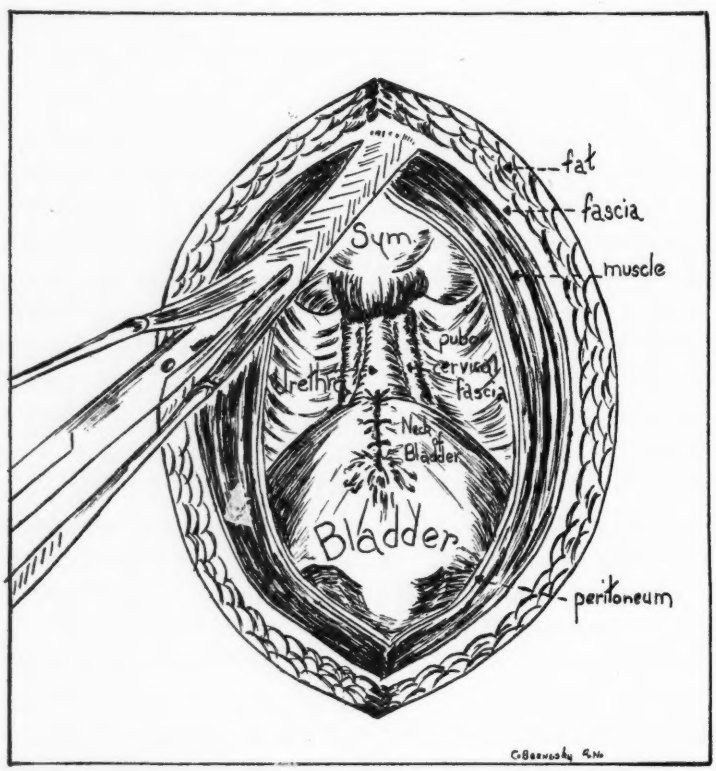

Fig. 1.—Schematic drawing showing the raising of the flap from the anterior rectus sheath and preliminary plication of the bladder neck. The pubocervical fascia can be seen on either side of the urethra.

CASE 3.—The patient was a 25-year-old para iii, who complained of severe stress incontinence and pains in the lower abdomen radiating down the legs and to the back. Examination disclosed an ovarian cyst about 8 cm. in diameter and a retroverted uterus but there was no urethrocele or cystocele to speak of. An oophorectomy and modified Gilliam hysteropexy were done in the usual manner after which the peritoneum was closed and a vesicourethral suspension carried out by the above technique.

The technique as previously stated is quite simple:

A No. 18 Foley catheter with 5 c.c. balloon is inserted into the bladder. After the bladder is emptied, the balloon is inflated, then gently drawn down until it impinges on the vesical neck, and strapped to the thigh with adhesive to maintain it at this point. The patient is placed in a partial Trendelenburg position and a suprapubic incision made from the umbilicus to the symphysis pubis down to the rectus fascia, which is cleansed of fat on either side of the midline for 1 or 2 cm. The abdominal wall is opened in layers, the incision in the fascia being made about 0.5 cm. to the right of the linea alba, the interrectal septum being opened and both rectus muscles exposed practically in their entirety. If a pelvic operation is to be done, it is carried out at this time, followed by a closure of the peritoneum, an added advantage of this technique being that it allows any operative procedure in the pelvis to be performed at the same time.

A strip of rectus fascia, a little over 1 cm. wide, is then cut free from the inner margin of the left external rectus sheath, beginning at the upper end and extending to within 1 cm. of the symphysis, where its attachment along with both pyramidalis muscles is preserved. This strap should be maintained as long as possible, since too short a strap is a handicap that cannot be overcome.

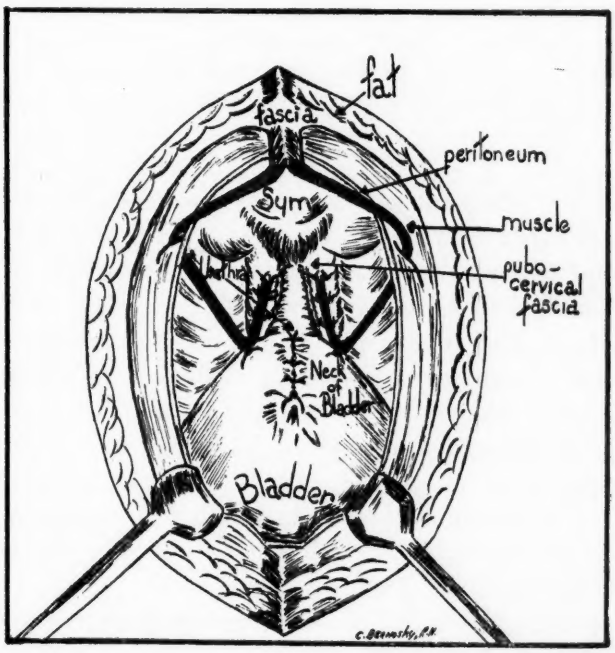

Fig. 2.—Schematic drawing depicting the position of the fascial strips after they have been sewed to the pubocervical fascia on each side of the urethra and to the bladder neck. The straps emerge from the abdomen through the lower portion of the rectus muscles to their attachment at the symphysis.

The anterior wall of the bladder with its pad of fat is now separated from the posterior surface of the symphysis by light pressure on top of the bladder and urethra with the fingers holding a sponge, this being easily accomplished since the suspensory attachment between the bladder and symphysis is quite delicate. The fascial strap is then split down the middle, so that each has a

pyramidalis muscle attached at its origin and the free ends are drawn through openings made in the middle of the rectus muscles by means of a Kelly clamp at the inferior portion where the muscular fibers join the tendinous part.

After plication of the fascia of the bladder neck with three or more mattress sutures of atraumatic No. 0 catgut, the fascial strips are now sutured to the pubocervical fascia, lateral to the urethra on their respective sides, the distal portion being sewed as far forward as possible and the part near the bladder neck being stitched also to this structure with one or two sutures of atraumatic No. 0 catgut. The amount of tension on the strips of fascia is best determined by trial, the suture first being placed into the fascial straps and then into the pubocervical fascia, the flaps being drawn down by the tying of the knots. There should be enough tension to elevate the urethra and bladder neck, but excessive tension should be avoided as this could conceivably cause strangulation at the site of the implantation with subsequent separation and pulling away of the flap. After the initial stitch has been tied and one is satisfied that the tension is just right, two or more additional sutures are placed on each side of the fascial strips so that they lie flat against the pubocervical fascia and maximum contact is effected. A cigarette drain is inserted into the space of Retzius and the abdomen closed in the usual manner. The catheter remains in situ for forty-eight hours after which it is removed. Urinary retention is rare and much less of a problem than in a comparable series of anterior-wall plastic repairs.

The average stay in the hospital was seven days. There were no morbidity and no complications. The postoperative results in all were excellent, each patient being completely continent when discharged from the hospital and follow-up data disclosed that they were still continent six months later.

Summary

A vesicourethral sling suspension operation should be the procedure of choice in those patients who have had previous unsuccessful vaginal operations for the relief of stress incontinence and in whom the dribbling of urine continues to be a serious and distressing symptom.

In those patients who present no cystocele or urethrocele to speak of, and yet whose primary symptom is stress incontinence, a vesicourethral sling operation usually offers the best approach to the problem.

When an intra-abdominal operation is indicated for pathology in the pelvis, a suprapubic sling suspension can be conveniently combined with the procedure and the stress incontinence relieved without resorting to vaginal surgery, provided the cystocele itself is not too extensive and does not cause other associated symptoms.

The urethral sling operation possesses many advantages besides that of being a purely abdominal operation. The fascial sling has the desirable virtue of being elastic and actually tightens during stress, since intra-abdominal pressure bulges out the lower abdominal muscles, causing the fascial strips to retract, thus elevating the vesical neck under the same conditions which previously had caused the structure to descend and allow urinary leakage.

The operation can readily be employed in young women during the childbearing age without fear that subsequent deliveries will break down the operative repair, as might be expected following vaginal plastic operations.

Conclusions

1. Three patients were operated upon by the technique described herein; no complications were noted, and all the operations were successful, since the stress incontinence was completely relieved in every case.

2. The operation is a departure from the extensive, time-consuming procedures previously employed and is relatively easy to perform.

3. It is felt that the principles of the operation are sound, and that it deserves further and wider acceptance as a worth-while procedure in the treatment of recurrent stress incontinence or in certain cases of primary stress incontinence where there is no associated cystocele or urethrocele.

4. The operation utilizes the rectus abdominis in addition to the pyramidalis muscles and attaches a sling in a position where it is likely to be most effective in providing a support to the sphincter of the bladder.

5. The preliminary plication of the bladder neck and upper portion of the urethra also narrows these structures in much the same manner as is accomplished by the vaginal route.

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MANAGEMENT OF HIRSUTISM IN THE FEMALE*

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HIRSUTISM is a condition characterized by abnormal growth of hair, especially in the female. Excessive hair growth may occur in men, but it is unnoticed except in rare instances, such as hypertrichosis universalis or dog men.[1] In such instances the hair growth over the face, back, and forehand is dysgenic,[2] resembling that of the aborigines of Australia, and has no obvious endocrine origin.

Abnormal hair growth in women naturally causes considerable emotional discomfort and not infrequently is their principal reason for seeking medical assistance. The management of such patients is the subject of this discussion.

Types

In spite of the fact that all patients have hair on their bodies, the various types and distribution of hair are generally accepted by most physicians with little inquiry into the normal and abnormal phases of hair growth. Advances in endocrinologic research have stimulated study of hair growth in relation to various syndromes which affect the female especially.

Hair growth on the body has been classified by Danforth[1] in three groups: (1) lanugo, (2) ambosexual, and (3) sexual. The first type is the very fine hair which covers the fetus and frequently persists for a few days postpartally. This hair growth may persist in adult life, as in dog men, but is usually lost within a few weeks following birth. A similar type, termed by Holzel[3] as transitional hair, appears in childhood in fairly constant distribution similar to that on the limbs or interscapular area of the adult and is replaced by final adult hair at puberty. Lanugo is generally believed to be unaffected by the endocrine system.

As the term implies, ambosexual hair is common to both sexes. Its distribution is confined to the axilla, pubic region, and scalp. This type is affected by hormones, however, and disappears or is reduced in quantity and thickness in such states as myxedema and hypopituitarism.

Sexual hair is the beard on the face and chin of males as well as the thick, coarse, bristly hair on their limbs, abdomen, and chest. The hair of the scalp may be considered to be sexual in the sense that in the male it is thicker and heavier, tending to regress in areas causing baldness or a receding forehead. These changes are apparently of endocrine origin since they do not occur after castration in the male.

*Presented at a meeting of the Louisville Obstetrical and Gynecological Society, Louisville, Ky., Feb. 22, 1954.

Rate of Growth

Factors influencing the rate of growth of hair include: (1) general bodily nutrition, (2) hormones, and (3) end-organ response.[4] In general, malnutrition decreases the rate of hair growth, but on the other hand obesity, although frequently associated with hirsutism, has never been considered an etiological factor. That hormonal stimulation affects the rate of growth of hair is well known, but which hormone is primarily responsible for hair growth has not yet been established. The steroids of the adrenal glands, especially those grouped as androgenic ketosteroids, are commonly believed to foster increased hair growth; yet the response of different individuals varies considerably. The end-organ response of the hair follicles to the other factors affecting hair growth is difficult to assess. The hair-follicle response, however, can be altered by irradiation and by the local application of drugs.

Incidence

How frequently does hirsutism in women occur? It has been estimated that 30 per cent of all women have heterosexual hair growth of some degree.[5] Most of these have only minor deviations from the normal which occasion no disquietude in the patient. Perhaps 10 per cent of these have sufficiently abnormal hair growth to cause them to enquire as to the cause.

Etiological Factors

Idiopathic hair growth is probably the commonest type occurring at puberty, during or following pregnancy, or postmenopausally. That which occurs at puberty or at the menopause is usually permanent, whereas that which appears at pregnancy usually disappears following delivery. Patients with idiopathic hirsutism often have a strong family history of increased hairiness and in our experience have been chiefly brunettes. Their racial antecedents may be of some help. The races which inhabit areas bordering on the Mediterranean, especially the southern Italians, Syrians, and Jews, are particularly prone to hirsutism.[6] Whereas Caucasian brunettes are more susceptible to increased hair growth, hirsutism in Negroes, the American Indian, and the Asiatic has rarely been reported. Obesity is common and psychogenic disorders are frequent. The genitals are normal and menstrual function is relatively normal. Holmer[7] assumed that in these hirsute women the Stein-Leventhal syndrome will develop but results of their endocrine studies are within normal limits.

A second type of hirsutism is due to a miscellaneous group of lesions such as thymic tumors, concussion of the brain, encephalitis, various forms of neuritis, and multiple sclerosis. This type may disappear following recovery from the primary lesion.

The third type of hirsutism is caused by adrenal disease. Excessive activity of the adrenal cortex from a tumor or hyperplasia causing oversecretion of the 11-oxysteroids or S steroids of Albright will result in Cushing's syndrome, with its well-known characteristics of hirsutism, obesity, osteoporosis,

altered glucose metabolism, and hypertension. The hirsutism in Cushing's syndrome is rarely as extensive as that of those diseases to be described later, and there are usually no evidences of masculinization. Bio-assays or chemical studies of urinary excretion products of these patients reveal an elevated cortin group. The 17-ketosteroid excretion varies widely but is often within normal range.

Perhaps included in the group caused by adrenal disease should be those pituitary lesions which might lead to hirsutism. Basophilic adenomas, originally described by Cushing, produce the identical picture of Cushing's syndrome, either directly or mediated through the adrenal. Similarly, excessive hair growth may be seen in acromegalic patients with no other demonstrable lesion. Another adrenal disease causing hirsutism is the adrenogenital syndrome. The hirsutism in adrenal disease is pronounced and there is definite evidence of virilization accompanied by defeminization. Bio-assays and chemical urinary studies, whether the cause is adrenal hyperplasia or an adrenal tumor, reveal an elevated 17-ketosteroid excretion rate with little or no change in the cortin excretion.

Finally, certain diseases of the ovary cause hirsutism in the female. Classed in this group are the Stein-Leventhal syndrome of multiple unruptured follicular cysts with disturbance of menstrual rhythm but no other evidence of masculinization. Ovarian tumors causing excessive growth of hair are arrhenoblastoma, adrenal cell rest of the ovary or luteoma, and hilar-cell proliferations manifested either as hyperplasia or tumor.

Management

The patient with hirsutism rarely complains of excessive hair growth, usually relating other associated complaints and relegating her abnormality to the background. Menstrual arrhythmia, or amenorrhea, is more likely to be the primary complaint. Many of these patients are embarrassed and talk about hair growth reluctantly. It is important to find out whether menses have occurred and when pubertal changes appeared. It is of interest to know something of the psychic adjustment of the individual at puberty, and whether she was a "tomboy" as an adolescent. Changes in weight during this period may be of some diagnostic value. It is also helpful to know the onset of excessive hair growth and baldness or other loss of hair. Occasionally, the demonstration of feats of muscular strength in adolescence will aid in the diagnosis of adrenogenital syndrome. On the other hand, profound muscular weakness suggests Cushing's syndrome.

If increased hair growth occurs prepubertally, especially with disproportionate rate of somatic and muscular growth, the adrenogenital syndrome must be strongly considered, whether the child be male or female. In the male, genital development with hirsutism prior to the average age of puberty suggests adrenogenitalism. In the female, the precocious advent of pubic and axillary hair is usually accompanied by hypertrophy of the clitoris and lack of concomitant secondary female characteristics.

Physical examination should be directed toward evidence of absence of the normal female secondary sex characteristics. In females with idiopathic hirsutism, the secondary sexual development is adequate, with female bodily contour, normally developed breasts, and muscular development of the average obese female. If hirsutism is associated with virilization, inspection reveals absence or underdevelopment of breasts, male fat deposits and muscular development.

Examination of the genitals may afford important clues. In addition to an escutcheon of male distribution, the clitoris and internal genitals furnish important information. Whereas the size and development of the uterus may be difficult to determine, enlargement of the clitoris may be definite. In patients with definite masculinization the clitoris is obviously enlarged. In many instances of hirsutism, however, the clitoris may be only slightly enlarged. Lesser enlargement or a normal clitoris tends to negate the possibility of a masculinization syndrome.

Laboratory studies of aid in the differential diagnosis include, of course, routine studies, such as blood count, urinalysis, and serology, but of more importance are the glucose tolerance tests and the excretion studies on twenty-four-hour urine specimens. Whereas abnormal glucose tolerance curves are usually present in Cushing's syndrome, they are much less commonly associated with adrenogenitalism, and probably are only casually related to ovarian diseases which cause hirsutism.

The 17-ketosteroid excretion rate is a valuable determination. Excessive excretion of 17-ketosteroids points strongly to the adrenal as the site of abnormality. Whereas the 17-ketosteroid excretion rate in ovarian tumors may be abnormal, the values are rarely significantly elevated. Excretion studies of cortin, other than to exclude Cushing's syndrome, aid little in the differential diagnosis. In those individuals who have elevated 17-ketosteroid excretion rates, further differentiation is possible, as suggested by Segaloff,[8] by means of infusion of compound F; 50 mg. is given intravenously over a period of twenty-four hours with the patient in bed, during which time the 17-ketosteroid excretion study is repeated. Wilkins[9] has previously reduced the rate of 17-ketosteroid excretion by administering cortisone. In those cases in which the elevated 17-ketosteroids of the patient are the result of hyperplasia of the adrenal cortex, a striking fall in 17-ketosteroid excretion will result, whereas there will be no change in the 17-ketosteroid excretion of patients with adrenal tumor.

Roentgenographic studies usually employed include roentgenography of the skull, kidney, ureter, and bladder and intravenous pyelography. Whereas many roentgenograms of the skull have been taken, few have yielded positive results. Intravenous pyelography, however, is valuable in detecting an abnormal position of the kidney resulting from a suprarenal tumor, if such be present. This, however, is not always conclusive and a retroperitoneal aerogram may be of further aid in delineating the adrenal gland. Unfortunately,

in many women with hirsutism an adequate aerogram is difficult to obtain because of obesity. The roentgenographic survey is of value also to demonstrate osteoporosis, a finding that would suggest Cushing's syndrome.

It should be recalled that some adrenal tumors cause hirsutism without other evidence of masculinization or alteration of menstrual function but with elevated 17-ketosteroid excretion, and these should be excluded by adequate study.[10] In hirsute women with amenorrhea but no definite evidence of virilization, the possibility of the Stein-Leventhal syndrome should be considered. It has been our policy at the Ochsner Clinic to perform exploratory laparotomy on such individuals who do not show conclusive evidence of adrenal disease. Of two similar cases, one whose preoperative studies strongly suggested adrenal disease actually had Stein-Leventhal syndrome whereas the other, thought most likely to have ovarian disease, had an adrenal tumor which could not be detected preoperatively. Careful exploration of the adrenal areas at the time of laparotomy for pelvic disease has, in the past, revealed several unsuspected adrenal neoplasms. These patients are then transferred to the surgical service for adequate therapy.

The hirsute woman with definite evidence of masculinization and a demonstrable adrenal tumor is treated on our surgical service. Such hirsute individuals with masculinization, whose 17-ketosteroid excretion responds to the infusion of compound F, have been treated by our endocrinologists by injection of cortisone with appearance of menses and of secondary female characteristics.

Results of Treatment

The advent of cortisone has done much to relieve the hirsute woman with adrenogenital syndrome. Assumption of menses, disappearance of acne, and disappearance of various male characteristics are impressive. Hair growth is retarded somewhat but unfortunately not altogether. Removal of adrenal or ovarian tumors which produce hirsutism likewise will lead to restoration of feminine characteristics and will cause some retardation in rate of hair growth with consequent improved psyche and general well-being. Unfortunately, the abnormal hair growth has never entirely disappeared in our patients. The parenteral or local administration of estrogens or other hormones has little or no effect on hair growth. Weight reduction is advisable but also will have little effect upon the hair growth. Psychogenic rehabilitation receives a tremendous boost with return of the normal menstrual function and with decreased frequency of shaving facial hair. Obesity is more easily controlled when psychic rehabilitation is adequate.

Therapy to eliminate hair growth must be directed toward destruction of the end organ. Electrolysis apparently is the most efficient and permanent means, although the more hirsute individuals rarely complete treatment. Depilation by other means is transient, and usually the patient employs a combination of these methods with the aid of cosmetics. Whereas cortisone therapy locally is efficient in reducing hair growth in animals,[11] its effect in the human being, excluding the adrenogenital syndrome, does not warrant its use either locally or generally.

Illustrative Case Reports

CASE 1.—Mrs. B. M., aged 39 years, had had amenorrhea for six years. One year after cessation of menstrual function she noticed hair growth over her face with recession of hair over the forehead. In addition, she began to gain weight slowly, resulting in a weight gain of about 75 pounds over the past four years. During the succeeding years her voice changed from soprano to baritone. The hair growth forced her to shave daily and caused her intense embarrassment. Between the ages of 13 and 30 years menstrual function had been regular at 28 day intervals lasting seven days. She had had three normal term pregnancies with children between the ages of 15 and 22 years. Laparotomy had been performed nine years before admission for an unknown cause.

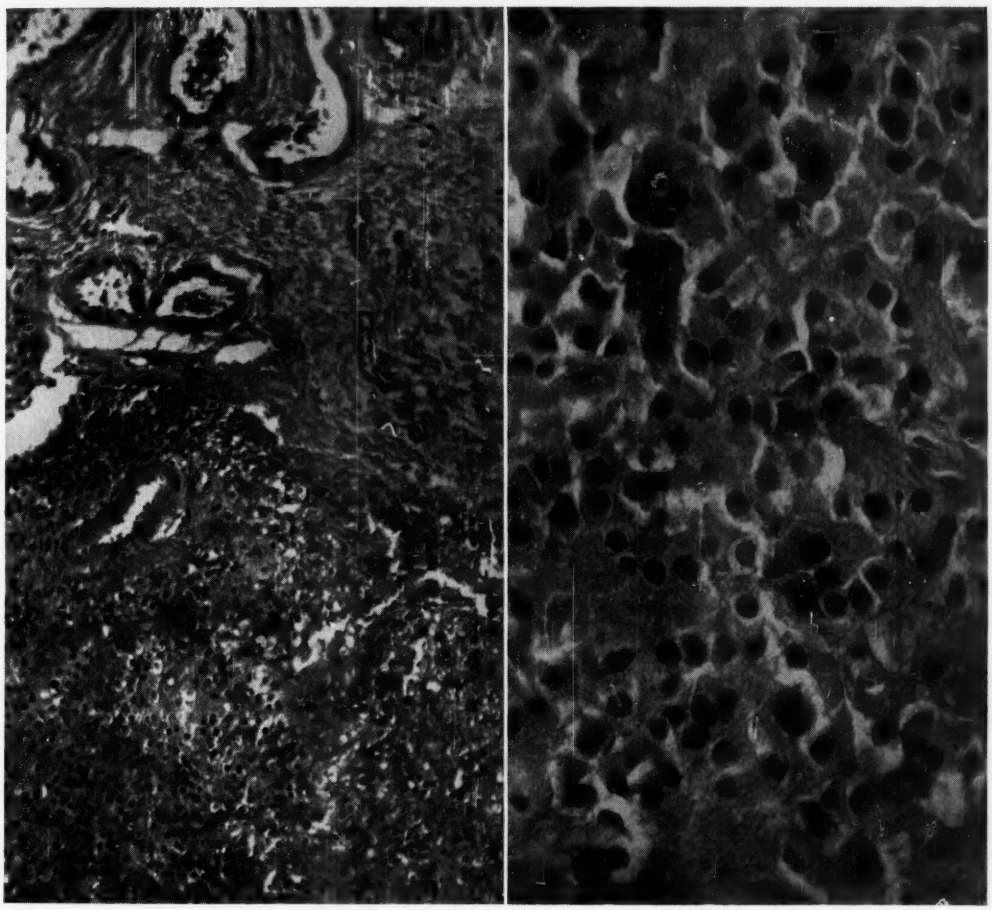

Fig. 1. Fig. 2.

Fig. 1.—(Case 1, B. M.) Section of ovarian hilar region with adjacent tumor. (×100; reduced ¼.)

Fig. 2.—(Case 1, B. M.) Section of tumor composed of polyhedral cells, granular cytoplasm with round nuclei of fine chromatin granules. These cells are identical with Leydig cells in the testis. (×450; reduced ¼.)

The patient weighed 203 pounds, was 5 feet, 4½ inches tall, and had a blood pressure of 150/110. Hair growth over the face and neck was profuse and there was increased hair growth over the entire abdominal wall, arms, and thighs. The clitoris was about twice as large as normal but the sizes of the other genitals were within normal limits.

Basal metabolic rate was minus 10 per cent and roentgenograms of the skull, chest, and lumbar spine, and excretory urograms showed no abnormalities. No evidence of displacement

of the kidneys was observed. Retroperitoneal aerogram or perirenal air insufflation was not performed. Although the fasting blood sugar value was within normal limits, glucose tolerance tests revealed a diabetic tendency. The 17-ketosteroid excretion rate varied from 15 to 22 mg. per 24 hours.

In the absence of definite evidence indicating an adrenal tumor exploratory laparotomy was performed. Palpation of the adrenal areas revealed no abnormality. A tumor about the size of a golf ball was found in the right ovary; the left ovary was normal. Both tubes had previously been resected. Total hysterectomy and bilateral oophorectomy were performed. Histologic examination revealed a hilar-cell tumor (Figs. 1 and 2).

Rehabilitation has been adequate but the patient must shave every two or three days. Some change in the voice has been noted but the size of the clitoris has remained unaltered. Hair over the abdomen and thighs has almost completely disappeared but the patient is still obese. Excretion of 17-ketosteroids has been only slightly reduced.

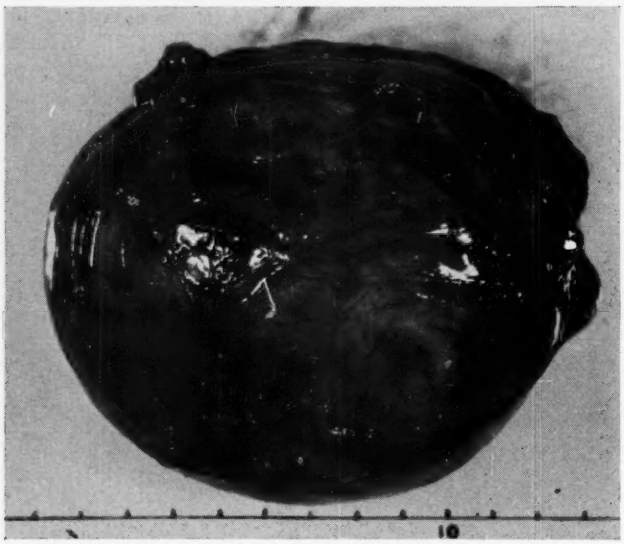

Fig. 3.—(Case 2, J. W.) Gross appearance of left adrenal tumor.

CASE 2.—Mrs. J. W., aged 29 years, first began to have amenorrhea at the age of 21 years and increased hair growth shortly thereafter. For the first five years this hair growth was not particularly troublesome but during the two years before admission it had increased sufficiently to require daily shaving. In addition, baldness with recession of hair in the temporal region had recently appeared.

The menarche occurred between 12 and 13 years of age and her periods were irregular with hypermenorrhea and polymenorrhea at the age of 18. She was treated for hypermenorrhea shortly before her last menstrual period at the age of 21. Although married for 4½ years, she had had no pregnancies and little libido. She had lost about 18 pounds in weight during the two years prior to admission.

Examination revealed diffuse hair growth over the face, chest, and abdomen with baldness on the occiput and recession in the temporal regions, an enlarged clitoris, and some acne. She weighed 117½ pounds, and blood pressure was 130/80. The pubic hair was masculine in distribution and the clitoris was 1½ inches long. Atrophic changes were noted in the labia but the internal genitals were within normal limits although the uterus was somewhat smaller than average. The sizes of both adnexa were within normal limits.

The basal metabolic rate was minus 3 per cent. The result of the glucose tolerance test was normal and repeated 17-ketosteroid excretion studies revealed from 450 to 600 mg. per

24 hours. Roentgenography of the chest and skull showed no abnormalities and an excretory urogram revealed displacement of the left kidney inferiorly although no calcification was noted in the region above the kidney to outline a definite adrenal tumor.

A preoperative diagnosis of adrenal adenoma was made and bilateral adrenal exploration with left adrenalectomy was performed. A large encapsulated tumor was removed (Figs. 3 and 4).

Following operation the hirsutism regressed, the female characteristics have returned, the breasts have increased in size, menstrual function has become normal, and the patient has had a subsequent pregnancy. Some reduction in the size of the clitoris has also been noted. Postoperative 17-ketosteroid excretion rates have been within normal limits.

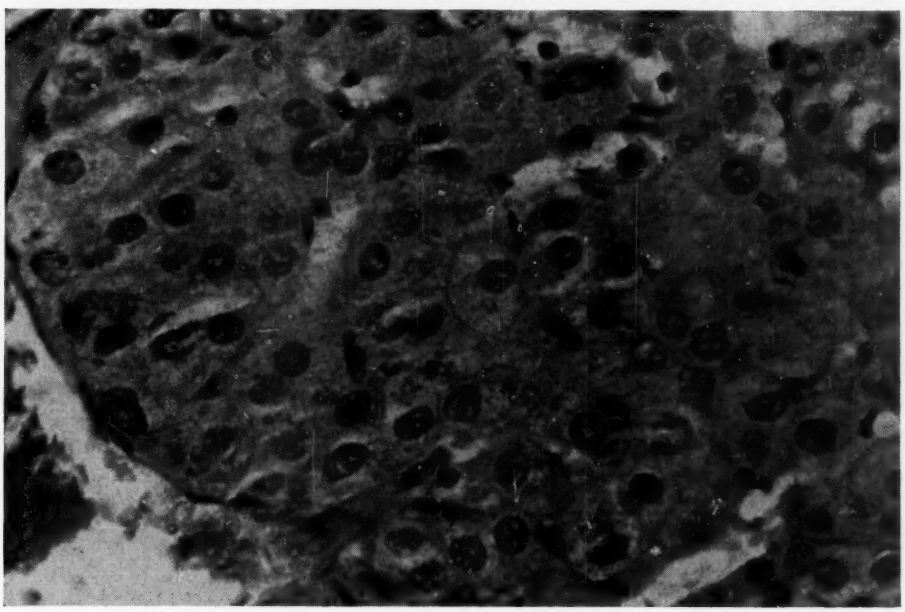

Fig. 4.—(Case 2, J. W.) Section of adrenal tumor, showing large polyhedral cells with abundant fine granular cytoplasm, scanty supporting stroma. The nuclei are finely granular with distinct borders. (×450; reduced ¼.)

CASE 3.—Miss M. B., aged 18 years, was referred to the Ochsner Clinic because of amenorrhea. Growth and development had been normal except for slight obesity in childhood. By the age of 13 she had grown to her present size. At that time excessive hair began to grow over the face and body but secondary sexual characteristics and the menses failed to appear. No change in voice was ever noted. Nevertheless, she has always been feminine, has enjoyed heterosexual company, and has a steady boy friend.

Physical examination revealed a young woman weighing 104 pounds and measuring 60½ inches with a blood pressure of 140/78. The breasts were completely undeveloped and muscular development was masculine. Hirsutism was apparent over the face, chest, and abdomen. Severe acne was also present. The clitoris was enlarged. Rectal examination of the other pelvic organs revealed them to be pubertal. The adnexa could not be definitely outlined.

Roentgenography of the chest and excretory urography showed no abnormalities. Urinalysis disclosed no sugar. Repeated 17-ketosteroid excretion rates revealed a maximum of 56 mg. per 24 hours and a minimum of 38 mg. per 24 hours.

A diagnosis of adrenocortical syndrome was made and under the influence of 50 mg. of cortisone, injected every day, the facial hirsutism has regressed considerably, the female sexual characteristics have appeared, including adequate breast development, and the acne has dis-

appeared. The patient has begun menstruating and has perfectly normal periods as long as she takes cortisone. Under the influence of cortisone the ketosteroid excretion rate has been reduced to normal levels. Hair growth has improved slightly but has not entirely regressed.

Summary and Conclusions

1. Hirsutism in the female, though rare, is a cause of psychogenic disability and may obscure a pathologic entity.

2. Lanugo is a fairly common form of hirsutism. When hirsutism extends to the ambosexual or sexual areas, thorough investigation is desirable.

3. Ambosexual and sexual hirsutism may be idiopathic, but diseases of the pituitary, adrenal, and ovary should be excluded.

4. Careful physical examination may aid in the differentiation of the types of disease leading to hirsutism.

5. Urinary 17-ketosteroid studies are indicated in all patients with moderate hirsutism. Patients with elevated values require further study. In the presence of features of masculinization, apparently normal values should be disregarded, pending further investigation.

6. Roentgenograms of the pituitary and renal areas, and retroperitoneal aerograms should be performed on all patients with an elevated 17-ketosteroid excretion rate to exclude pituitary and adrenal neoplasms.

7. Chemical studies of the blood glucose levels and cortin excretion help to exclude Cushing's syndrome.

8. Exploratory laparotomy with exploration of the adrenal areas is recommended for those patients with hirsutism in whom a satisfactory diagnosis cannot be made.

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PUBLIC RELATIONS AND MEDICINE*

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I VENTURE the opinion that medical contribution to the welfare of mankind in the last two decades has been greater than that of any similar period in history. Life expectancy has been increased to such an extent that old age has become a social problem. Geriatrics, a newly coined term for a new specialty, is to a large extent the result of this medical progress. On the individual level, we see untold numbers of brilliant medical men in full-time research and/or in teaching posts—in spite of low salaries. An example of professional devotion on the part of an individual is the recent decision of Dr. Charles W. Mayo to withdraw his name as a candidate for the U. S. Senate. The reason given by him to the press was that he preferred medicine to politics. Probably the highest example of a life dedicated to humanity through medical service is that of the noble and Nobel prize winner, Dr. Albert Schweitzer. At the age of 32, already recognized in the world of music, he decided to study medicine. Relinquishing fame and fortune, he assigned himself to the primitive life of a medical missionary in Africa.

In spite of these facts, public relations are at an all-time low. Current lay-press medical reporting is inflammatory and disturbing. The doctor and medical practice in general are receiving adverse publicity. Obstetrics and Gynecology have the dubious distinction of being delegated as the official whipping boy. The following examples illustrate the special attention we are receiving: The *Redbook* of February, 1954—"How safe is childbirth by surgery? Tens of thousands of unnecessary cesarean sections are performed each year. Much of this is attributed to physicians who are interested only in higher fees." *Cosmopolitan* magazine, October, 1953—"Hysterectomy—The tragic and shocking truth about an operation needlessly performed on thousands of women each year." The *Reader's Digest* of August, 1953, headlined an article on the same subject as follows: "Hysterectomy: Medical Necessity or Surgical Racket?" The last two articles quoted authority and statistics taken from *The Journal of the American Medical Association* and the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY.

Fee gouging and fee splitting receive considerable attention, again castigating the same whipping boy. A one-half page advertisement in the *Philadelphia Evening Bulletin* on Friday, Oct. 16, 1953, was headlined in two-inch type as follows: "Why Some Doctors Should Be in Jail." Below, in smaller type, readers were advised to look for a forthcoming article in *Collier's* magazine. This article appeared in the issue of Oct. 30, 1953. The cover page was given the same treatment as the newspaper advertisement with the addition

*Presidential Address, presented at the Obstetrical Society of Philadelphia, May 6, 1954.

of two full figures in color of gloved and gowned surgeons with caps and masks. Quoting from this article on why some doctors should be in jail: "The practice of fee splitting is sufficiently widespread, particularly in the field of gynecologic surgery, to have led to the coining of the term 'the rape of the pelvis.'" George E. Sokolsky, a nationally syndicated columnist, on March 3, 1954, wrote this masterpiece in the *Philadelphia Inquirer:* "I heard a story the other day of two young people about to have their first child. They were referred to a specialist. There were no complications in the case, except the fee asked, which was $750, including prior and after treatment. The young people were bankrupted by their first child"—an example of the worst form of irresponsible reporting. By his own admission, the story is only hearsay.

Originally I intended limiting quotations of poor press notices to those reflecting on the medical profession. I cannot resist, however, quoting an attack on an allied profession—nursing. The following is from the *American Weekly,* a nationally syndicated Sunday newspaper supplement, issue of Nov. 15, 1953: "What has happened to our nurses? A nation wide survey reveals that too many patients are left to the untender mercy of lazy, tip seeking novices and incompetents."

Freedom of the press is one of the basic foundations of our civilization. Scientific freedom is equally basic. Medicine lives by its professional freedom and jealously guards it. These privileges carry with them responsibilities, however. That applies both to the press and the medical profession. Democracy thrives on controversy, but the type of news reporting quoted above is neither news nor controversial. It is pure and unadulterated propaganda. It is slanted and vicious. It appears to be organized and have specific direction and purpose.

We are charged, among other things, with gouging fees, unnecessary surgery, and fee splitting. As for gouging fees, let us examine the facts. The *New York Times* on Jan. 24, 1954, quoted President Eisenhower's message to Congress to the effect that the total private medical bill of the nation exceeds nine billion dollars a year. Of that amount, 37 per cent is estimated as doctors' cost. Divided among 200,000 physicians, the average gross income amounts to about $16,000 a year with an approximate net income of $10,500. Are these statistics consistent with widespread fee gouging?

As to fee splitting and unnecessary surgery, it *is* a matter of record that some of the leaders in organized medicine admit the existence of, and have cried out against, these evils. Twenty-three states recognize the existence of fee splitting in that they have enacted laws against it. To the best of my knowledge, however, no one has ever been convicted on this charge. Condemnation of these practices by official representatives of organized medicine will not satisfy public opinion, nor will unenforced legislation. It calls for a more resolute and dynamic program of action by organized medicine on both the national and local levels. We must make every effort first to determine the extent of these problems and then to take necessary steps to correct them.

The poet and the novelist are also potent mediums of public information. Among them are many physicians. Most authors are inclined to portray a more rounded and complete characterization of doctors and medical practice. A recently published novel, *Not as a Stranger,* by the late Morton Thompson, is a good example. He depicts various types of physicians from one extreme to the other, not omitting the variations between.

Let us take a closer look at the doctor in fiction. Let us see how we are judged by our colleagues in the field of writing. And finally, let us see how we respond to these critics.

Dr. William Carlos Williams, a graduate of the University of Pennsylvania, class of 1906, until his recent retirement was a successful and busy practitioner in Rutherford, New Jersey. All of his life he was a student of the Muse and today his writing is evaluated, in some quarters, as being most representative of modern poetry and most likely to live on as a classic example of the modern school. Quoting from his autobiography, "There are good doctors and bad doctors: you can't tell them by their names; thieves, even murderers, with the most respectable names. On the other hand there are the most painstaking and humane priests of healing. . . . There are financial geniuses . . . men who could well give our Morgans and Rockefellers points on how to improve the complexion of a nickel. . . . There are also men and women who pain over every dollar they charge the sick for their cure and live virtually poverty-stricken lives of devoted service to mankind—which doesn't on the other hand make them the best doctors by any means.

"It's a strange thing how many phases go into the making of a good, serviceable physician. Some have hands, just good surgeon's hands, and if by luck they have a head and a heart to go with them, they can reach the heights. Others are a menace to the community they inhabit. How are you going to tell them apart?"[1] Certainly an honest and well-balanced sketch.

An example of an entirely different type of writing is taken from the *Collected Poems* of the late Dylan Thomas. It is a delightful satire called "On Hygiene":

> "Of old when folk lay sick and sorely tried
> The doctors gave them physic, and they died.
> But here is a happier age: for now we know
> Both how to make men sick and how to keep them so."

The doctor makes a good subject for satire and caricature. The artist frequently takes what is called artistic license. He exaggerates what he sees and feels. I believe that the public intuitively responds to it in like manner. It is not propaganda. It may be offensive but is rarely vicious.

In March, 1953, Dr. Robert A. Kimbrough, Jr., a former president of this Society, in collaboration with Agnes M. Kimbrough,[2] published a paper titled "The Physician in Current Fiction." The following quotation from their

introductory remarks is interesting: "We cannot expect the fictional portrait of ourselves to be flattering; the style today is candid. We may, however, expect the portrait to be fair because of the presence of physicians in the field of writers. . . . It would be an impertinence for us to like or dislike what they have made of us, since we have been their models, and since the resultant portrait is, for better or worse, the composite image which represents us in the lay mind."

The late and great Dr. John Chalmers DaCosta[3] read a paper titled "Dickens's Doctors." The following are his concluding remarks: "Such are Dickens's doctors—fools, drunkards, blackguards. . . . Most of his pictures are broad caricatures in which a single failing is exaggerated into the essential part of the man. Truly, as a general thing, he has not been complimentary. Let us profit by the sketch."

The speeches of Dr. DaCosta are a rich source of information on doctors and medical practice as he observed them. I shall quote from his published speeches more or less haphazardly.

"Some men leave the profession because they did not reach the top. There was no elevator and they were too lazy to climb."

"One of the earliest discoveries made by a recent graduate is that some members of the medical profession possess marvelous powers in dealing out personal detractions and great versatility in selecting subjects for it."

"A man may operate with admirable dexterity and yet do very bad surgery, operating perhaps when no operation should be done, or removing, maybe most skillfully, what ought not to be removed."

In conclusion, basically the cause of existing poor public relations in connection with medicine is the economic factor. Medical costs have risen to a point beyond the ability of the average American to pay. The health of the nation is naturally of paramount interest to the government. Kept out of the hands of politicians and bureaucrats, the resolution of this problem would not seriously affect the high standard of medical practice. The threat is that this has become a political pawn. To salvage the situation calls for high-level statesmanship.

All other possible causes are secondary; for example, overemphasis on specialization and concentration of specialists, leading to keen competition and its resultant evil practices. This further leads to depletion in the ranks of general practice, which in turn results in the family physician not having sufficient time to function in his traditional capacity as family counselor, healer, and confidant.

The view just expressed may be a short view, for in truth, medicine has expanded its horizons. Our age of specialization may be only the forerunner of the time when the all-inclusive subject of medicine will be broken up into its various component parts. Whether the long or the short view is correct, I frankly do not know. The correctness of one does not necessarily preclude the correctness of the other. Certainly, at the present time, immediate and obvious problems should be surveyed and, if possible, remedied.

We are living in an era of materialism and turmoil. It is more imperative than ever that we maintain our traditional high standard of values. What the future holds in store, no one knows. But of one thing we may be sure: like the weather, medicine is here to stay.

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Department of Case Reports
New Instruments, Etc.

INTRATUBAL TWIN PREGNANCY WITH RUPTURE

Review of Literature and Presentation of a Case

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TWIN ectopic pregnancy is a condition which occurs far less frequently than the more commonly described single ectopic pregnancies. The twins may be in the same tube, one in either tube, one in the tube and one in the uterus, or one in the tube and one in the ovary, or abdominal cavity. Combined extrauterine and intrauterine pregnancy is the most common combination, followed by twin pregnancy in one tube, the rarest of all being bilateral simultaneous twin pregnancy, with one of the twins in each of the tubes. Even more rare, cases of multiple ectopic pregnancy such as triplet pregnancy have been reported,[1] and there has been one case of quintuplets recorded.

The first case of twin pregnancy in one tube found in the literature was reported by De Ott[2] in 1891. Since that time, others have described similar cases. The first attempt at a review of the literature was made by Arey in 1923,[3] at which time he collected 40 authentic cases of unilateral twin tubal pregnancies. In 1938, Falk and Blinick[4] again reviewed the literature and, including two cases of their own, felt that there were 65 authentic cases. Since that time, we have been able to find 9 papers[5-13] in the English language journals in which cases of unilateral twin pregnancies are described, the most recent[13] being in June of 1950. Although the figures for the total number of authentic cases vary, the most likely number is 78 prior to this report. Only one paper, that of Trolle,[12] estimates a greater number. This author stated that about 100 cases had been reported up to that time (1948) but he did not give any authentication for this figure. His argument that some cases have occurred without appearing in the literature is, however, undoubtedly true. The paucity of such cases is borne out by the fact that reviews of fairly sizable series of ectopic pregnancies fail to report a single case of unilateral twin tubal pregnancy.[14-17]

We believe that, including the case recorded, there are 79 authenticated cases of unilateral twin tubal pregnancy.

Preoperatively, unilateral twin tubal pregnancy cannot be differentiated from a single tubal pregnancy and the management of these patients will be identical with the management of any patient with an ectopic pregnancy. The age

incidence, most cases occurring in the third decade, and the history of relative sterility are seen in patients with twin tubal pregnancy in the same proportion as with single ectopic pregnancy. Tubal abortions are more frequent than tubal ruptures in both conditions. A history of twins in the family is not always found, although in the case presented there were twins in the same generation. There is no essential difference in the mortality rate for twin tubal pregnancy as compared with that for single ectopic pregnancy, which has been reported to vary from 2.29 per cent[18] to 4.6 per cent.[19]

The tubal pathology does not differ from that in other varieties of ectopic pregnancy. Most of the twins have not been examined in an attempt to differentiate between a monozygotic or dizygotic origin, and in many cases the differentiation must be difficult. At least two cases of dizygotic twins have been described. These were reported by Haukohl and Anderson[11] and by Trolle,[12] both of whom cite as evidence for this contention the fact that both pregnancies were of definitely different ages, suggesting individually fertilized ova. A different rate of development, for reasons unknown to us, could equally well explain the difference in the apparent age of the two pregnancies, but one cannot deny the possibility that a dizygotic origin could be the proper explanation. In the case presented herein it is probable that the origin of the pregnancy was from a single ovum.

Case Report

The following is a report of a case representing a typical example of unilateral twin tubal pregnancy.

The patient was a 33-year-old white woman who was admitted to Stewart Air Force Base Infirmary on Dec. 29, 1953. Her last menstrual period was on Oct. 18, 1953, and she had noticed some nausea but was not aware that she was pregnant. Her previous menstrual history was completely normal. Three years previously a complete medical evaluation had been performed because of a mild anemia. In the face of normal results, she was treated with iron and liver to which she responded well. Her only previous operation was a tonsillectomy. She had been married one and a half years and was never pregnant. First cousins on her paternal side were twins.

At 4 P.M. on Dec. 29, 1953, she began to have rather severe, steady lower abdominal pain. She disregarded the pain and ate a full dinner which she promptly vomited. She vomited repeatedly after that and noted that the pain spread to involve the entire abdomen. At 11 P.M., after seven hours of pain, she entered the hospital.

Physical examination on admission revealed a well-developed and well-nourished woman in obvious, severe distress from abdominal pain. She was pale and any motion produced pain. The pulse was 100, blood pressure was 88/60, respirations were 22 and shallow. Her general physical examination was within normal limits except for the abdomen. The abdomen was markedly distended and tense. It was diffusely and severely tender throughout but more so in both lower quadrants. There was rebound tenderness in all quadrants, greatest in the right lower quadrant.

A tentative diagnosis of a ruptured ectopic pregnancy was made. The patient's blood was typed and cross-matched and the operating room was prepared. Pelvic examination at that time revealed marked fullness of both the anterior and the posterior fornices which were bulging and extremely tender. Complete examination was not possible because of the marked abdominal spasm but there was definite evidence of a mass present in the right tube.

With this confirmation of the diagnosis, the patient was taken to the operating room and exploration made through a right lower rectus muscle retracting incision, the peritoneal cavity being entered just to the right of the midline. The anesthetic* used was Pontocaine, 16 mg., given as spinal anesthesia and supplemented with intravenous Pentothal. When the peritoneal cavity was opened, clotted and liquid blood was seen throughout and there was considerable blood staining and edema of the greater omentum which was down in the pelvis. Immediate attention was directed to the right tube which was found to be distended in its ampullary portion to a size of approximately 4 by 8 cm. This enlarged, rounded area was dark purple and on its superior aspect there was a small opening from which there was active bleeding and through which protruded a small but well-formed embryo approximately ten weeks of age. As expeditiously as possible, the right infundibulopelvic ligament was ligated as was the broad ligament. The tube was then transected at the uterine angle and the tube and ovary on that side were removed. The rapid control of the active bleeding restored the patient's vital signs to normal and only one unit of whole blood was administered during the procedure. Upon inspection of the removed right tube, gross hemorrhage was seen within the wall of the tube at the site of rupture. Through this opening protruded placental tissue. A second embryo, in every way similar in size and shape to the first one, lay within the cystic dilation of the tube. No apparent separation between the two amniotic cavities could be made out although two umbilical and placental areas could be seen.

The uterus was of normal size and position but the left tube was completely blocked at its fimbriated end and distended in its mid-portion to a size of about 2 by 3 cm. This, too, was purple and cystic in nature and it was suspected that a hematosalpinx was present. For this reason a left salpingectomy was performed. Care was taken to preserve the left ovary. All raw areas were reperitonized and then as much of the clotted blood as possible was removed from the peritoneal cavity. The wound was closed with the use of chromic catgut for the peritoneum and fascia and silk for the skin.

Postoperatively the patient rather rapidly developed abdominal distention and vomiting. A paralytic ileus was suspected and a Miller-Abbot tube was inserted. Attempts at passage of this tube through the pylorus were unsuccessful, in spite of repeated fluoroscopically controlled trials. The tube continued to serve merely as a gastric suction apparatus. X-ray examination of the abdomen on the third postoperative day revealed marked dilation of the entire colon and several loops of small bowel. Continued treatment with enemas, Prostigmin, and Urecholine parenterally as well as castor oil by mouth succeeded in overcoming the ileus and on the fifth postoperative day the Miller-Abbot tube was removed, and the patient started on oral feedings. She tolerated this well and from that time on made a rapid recovery. Two transfusions were necessary in the week after surgery because the hemoglobin had fallen to 8.5 Gm.

During the patient's hospital stay, she had mild vaginal bleeding which lasted for about two weeks after the operation and then subsided. At examination four months after surgery, she was in excellent health and had returned to her normal activities.

Pathologic examination† of the two tubes and the right ovary revealed a tuboovarian mass measuring 8 by 4 by 4 cm. The ovary was grossly normal and microscopically consisted almost entirely of a corpus luteum. In approximately the center of the right oviduct there was noted a defect measuring 3 cm. in length through which protruded spongy, tan placental tissue and two embryos measuring 4 cm. in length. Sections of this oviduct showed it to be dilated and thin-walled, with masses of placental villi, decidua, and clot attached to its inner surface.

The left oviduct was 6 cm. in length but was dilated to about 2 cm. in diameter. The wall was thickened and the lumen was smooth, shiny, and golden yellow in color.

It was the pathologists's opinion that the specimen represented a ruptured twin tubal pregnancy and that there was a chronic salpingitis of the left tube.

*Administered by Anthony Bucalo, First Lieutenant, USAF (MC).
†Performed by W. J. Redner, Captain, USAF (MC).

Summary

1. A case of unilateral twin tubal pregnancy is reported.

2. After a review of the English language literature, it is believed that this is the seventy-ninth reported case.

3. Similarity to single ectopic pregnancy has been discussed and the features peculiar to the twin pregnancy elaborated.

4. The importance of the examination of the contralateral tube is emphasized.

I wish to express my gratitude to Robert F. Jones, Captain, USAF (MC), Commander of the 612th USAF Infirmary, Stewart Air Force Base, for permission to report this case.

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UNRUPTURED PRIMARY OVARIAN PREGNANCY

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PRIMARY ovarian pregnancy is the rarest of all ectopic gestations. It is reported to occur once in 25,000 pregnancies. The actual incidence, however, is probably unknown, since a number of large institutions have not reported this entity. There are also conflicting reports in the literature as to the total number of "authentic cases" to date; these range from 125 to a little more than 200. The discrepancy is due to the individual interpretations of the criteria laid down by Spiegelberg in 1878, namely, (1) that the tube on the affected side be intact, including the fimbriated end; (2) that the fetal sac occupy the position of the ovary; (3) that it be connected with the uterus by the ovarian ligament; and (4) that definite ovarian tissue be found in its wall. It is then obvious that strict adherence to Spiegelberg's original criteria, or modification thereof, is necessary.

From various sources, Wittenberg and Reis calculated the incidence of ovarian pregnancy as one in 117 of all ectopic gestations. This comes very close to 1 in 110 ectopic pregnancies at the Free Hospital for Women, as reported by Isbell and Bacon. At the Cincinnati General Hospital, over a twelve-year period extending from Jan. 1, 1941, to Dec. 31, 1952, there were 201 ectopic pregnancies out of 36,777 deliveries, which include term and premature deliveries and abortions of all types. This gives an incidence of one ectopic in 183 pregnancies, a figure somewhat higher than the incidence (one in 200 to 300) generally quoted. This is probably due to the high incidence of pelvic inflammatory disease among our Negro patients.

We make no attempt to explain or postulate the cause or mode of implantation in ovarian pregnancy. The cortical or surface implantation of Meyer and Novak, the intrafollicular implantation as taught by Leopold, and the interstitial or juxtafollicular fertilization are all conjectural but definite possibilities. We agree with Meyer and Wynn that "reports of single cases are not needed for the purpose of emphasizing the occurrence of ovarian pregnancy, yet such reports nevertheless may help in the determination of the relative frequency of this novel and sinister condition, and also throw further light upon its genesis and the finer relations of the implantations, as well as upon other matters." It is with that purpose that our case is presented.

R. W., 20 years old, a Negro woman, was admitted to the hospital from our Gynecology Clinic on Nov. 13, 1953, with the diagnosis of possible ectopic pregnancy. Her chief complaints were pain in the right lower quadrant of the abdomen and vaginal bleeding. Her past history included measles, chicken pox, and whooping cough in early childhood, and pneumonia at 13 years of age. The menarche occurred at the age of 12. The menstrual periods had been fairly regular, lasting 5 days, with moderate flow, accompanied by mild

cramps and at times nausea and vomiting. Her last normal period was in mid-August. From October 12 to 17 she had slight vaginal bleeding, and another but more profuse episode occurred from October 20 to November 10. Three weeks prior to admission she began to have a dull aching pain in the back radiating to the right lower quadrant of the abdomen. Besides amenorrhea in September, other signs and symptoms of pregnancy had been absent.

Fig. 1.

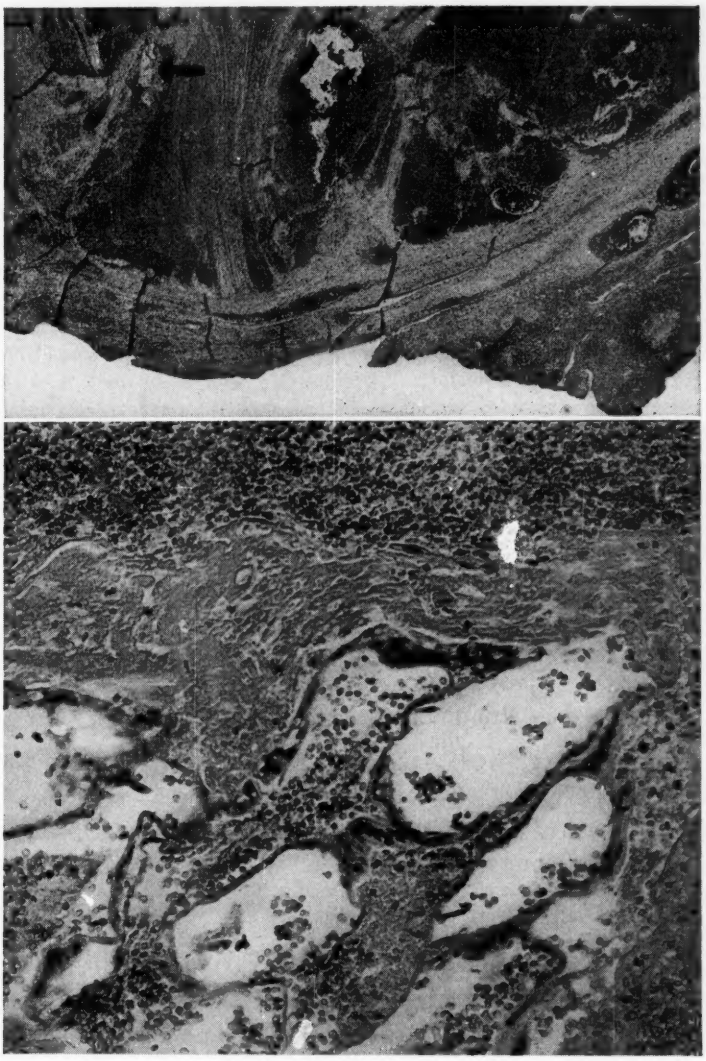

Fig. 2.

Fig. 1.—Low-power view of resected ovary and hematoma. At the right below is ovarian stroma. The arrow points to a cluster of blood vessels and trophoblastic tissue, shown in the next photograph under higher magnification. (Hematoxylin and eosin. ×40; reduced ⅙.)

Fig. 2.—Higher-power photomicrograph of the group of blood vessels designated by the arrow in the preceding photograph. Syncytial cells are apparent. (Hematoxylin and eosin. ×200; reduced ⅙.)

Physical examination revealed a fairly well-developed and fairly well-nourished patient in no acute distress. The temperature, pulse, and respirations were normal; the blood pressure was 120/80. The rest of the examination was negative except in the right lower quadrant of the abdomen where slight tenderness to deep palpation was elicited. Pelvic examination showed normal external genitals and a nulliparous cervix which was firm and

normal in color but moderately tender on manipulation. The uterus was felt to be slightly enlarged and in anterior position. A tender, semicystic mass, about 3 by 3 cm., was felt in the right adnexa; the left adnexa were clear. There was slight vaginal bleeding.

Laboratory determinations: hemoglobin, 13.5 Gm. per 100 c.c. of blood; leukocytes, 7,950; urine normal. On the second day, hemoglobin, 12.5 Gm.; leukocytes, 9,150; urine negative. An anteroposterior film of the abdomen was negative. The Friedman test was not done.

Diagnosis: possible intrauterine pregnancy with corpus luteum cyst or ectopic pregnancy on the right.

For the next two days the patient was afebrile and continued to have vaginal spotting. Pain in the lower abdomen was the outstanding complaint. A pelvic examination was again done on the third day and the previously described mass was still felt and tender. An exploratory posterior culpotomy was done the next day. After the cul-de-sac of Douglas was opened, a bluish-colored right adnexal mass was exposed with difficulty. Attempts to bring down the posterior surface of the fundus with tenacula for visualization of the adnexa were unsuccessful because of the narrow vagina. Under direct palpation the mass was felt to be bigger than on previous pelvic examinations. An exploratory laparotomy was done, which showed no free blood in the peritoneal cavity. The right ovary measured 6 by 6 by 5 cm., was mottled black in color and entirely free of adhesions with no evidence of rupture. The right tube, including its fimbriae, was grossly normal and retained its normal anatomical position. The uterus was of normal size, in mid-position, and the left tube and ovary were normal. An attempt to conserve ovarian tissue was impossible, and oophorectomy was done.

On examination of the removed specimen, a fragile cystic mass of dark clotted blood surrounded by a thin, white, fibrous capsule was seen. The center of the mass was occupied by a small translucent sac measuring 1 by 1 by 0.5 cm. The wall of this sac was composed of two membranous layers which contained dark blood. A dense layer of ovarian tissue surrounded the hematoma. No recognizable follicles or corpus luteum were seen in the immediate vicinity of the hematoma but were present in some pieces of ovarian tissue obtained from near the pedicle of the ovary. Diagnosis: ectopic ovarian pregnancy.

The patient had an uneventful recovery and went home on the tenth day.

Summary and Conclusions

1. The number of reported cases of primary ovarian pregnancy to date is approximately 200. The actual incidence is unknown.

2. Strict adherence to Spiegelberg's original criteria, or a modification thereof with universal concurrence, is essential.

3. A careful microscopic examination should be made of ovaries showing hemorrhagic lesions similar to endometrial or chocolate cysts, hemorrhagic corpus luteum cysts, and other similar gross ovarian pathology.

4. A case of primary ovarian pregnancy, the first one to occur in this institution, is presented. The probable mode of implantation was either cortical or interstitial.

We wish to express our appreciation to Dr. Herbert Braunstein of the Department of Pathology for his assistance in preparing the slides and photographs.

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Department of Reviews and Abstracts

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Selected Abstracts*

Acta obstetricia et gynecologica scandinavica

Vol. 33, Fasc. 1, 1954.

Brandstrup, E., and Schou, Per: Ten Years' Caesarean Sections in Denmark, 1941-1950, p. 1.

Stamer, S.: Course of Labour in Elderly Primiparae, p. 16.

Westgren, A.: Placenta Praevia. A Clinical Study of 350 Cases Seen in Stockholm During the 10-Year Period, 1940-1949, p. 29.

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Abolins, J. A.: Nursing and Temperature of the Breast, p. 60.

*Wist, A.: The Relationship of Endometriosis to Tubal Pregnancy, p. 69.

Wist, A.: Decidual Reaction and Tubal Pregnancy, p. 83.

Samuelsson, Stig: Rupture of the Utero-ovarian Veins During Pregnancy and Labour, p. 91.

Ryden, Ake B. V., and Westren, Anders: Inflammatory Complications of Hystero-Salpingography and Their Prevention, p. 109.

Wist: The Relationship of Endometriosis to Tubal Pregnancy, p. 69.

A comprehensive review of the literature relating to endometriosis of the tube as an etiological factor in tubal pregnancy is presented. The author credits Webster in 1896 with being the first to describe endometrial tissue in a tube and to postulate these endometrial areas as possible implantation sites for the fertilized egg. The finding by Philipp and Huber in 1939 of endometriosis in 44.9 per cent of the tubes of 616 patients has impressed Dr. Wist greatly. In the series quoted, endometriosis was found almost always to be situated in the interstitial portion of the tube. The material presented by Dr. Wist consists of 104 pregnant tubes in 5 of which endometriosis was found (5 per cent). Endometriosis is very rare in the ampullar and distal isthmic portions of the tube but is relatively common in the interstitial portion. "Tubal endometriosis alone offers a natural explanation for the aetiological mechanism of interstitial pregnancy. . . . It is very probable that the majority of interstitial pregnancies are produced as a sequel to tubal endometriosis." The author feels, however, that, in the over-all picture, endometriosis of the tube is of secondary importance as an etiological factor in tubal pregnancy.

JOSEPH J. SMITH, M.D.

Vol. 33, Fasc. 2, 1954.

Bergman, Per, and Sjostedt, Sven: Heart Disease in Pregnancy, p. 117.

Werko, Lars: Pregnancy and Heart Disease, p. 162.

Svenstrup, Carl: Small Cysts of the Ovary, p. 211.

Vol. 33, Supp. 1, 1954.

*Morstad, Odd: Birth Injuries (A Follow-Up Examination).

*Titles preceded by an asterisk are abstracted below.

Morstad: Birth Injuries, Supp. 1.

A birth injury "may be defined as an unfavorable concurrence of external and internal factors—a failure in the correlation between stress and adaption—resulting in temporary or permanent functional disturbances in the infant." Morstad feels the obstetrician is primarily responsible for a large percentage of birth injuries, and the pediatrician responsible for the injured child, hence the problem of birth injuries belongs to both obstetrician and pediatrician. From an obstetrical point of view, two main groups of injuries occur: (1) injuries which do not differ from those which may occur at any time during postnatal life; and (2) injuries which give rise to structural or functional disturbances meriting special attention when occurring during childbirth.

A well-documented historical sketch of cerebral palsy and brain damage due to asphyxia and trauma is presented. A number of important points not stressed in the American literature have been reviewed. Beneke in 1910 made a comprehensive study of the pathoanatomical conditions in cerebral hemorrhage with special reference to injuries of the tentorium cerebelli. These tears were a frequent occurrence but were often overlooked. He also demonstrated lacerations following entirely normal deliveries. Roberts, in 1925, pointed out the significance of spinal fluid findings and the difficulties encountered in their interpretation. In 423 lumbar punctures of normal babies, colorless fluid was never found; there was always some degree of yellowness, the intensity having no relationship to the difficulty of the delivery or to the condition of the infant at birth, but depending on the degree of physical development. Of 60 cases in which lumbar puncture revealed intracranial hemorrhage, only 26 had presented clinical signs of this condition.

Factors of great importance in relationship to birth injuries appear to be prematurity, breech deliveries, and operative deliveries. How long a patient should be allowed to labor is indeed a difficult question to answer even today, when we are armed with x-ray pelvimetry and a number of interesting indices. Often the difference between a normal infant and one with a birth injury such as asphyxia depends upon the niceties of judgment of the most seasoned obstetrician.

The suggestion of Bloxsom that a special regimen for infants with cerebral injuries be set up on the same basis as that for the premature deserves consideration. Segregation in a separate ward under the permanent care of a trained specialized staff would undoubtedly decrease the mortality rate as well as secure the greatest functional result from the existing pathological condition.

The present study originated from the University Maternity Hospital of Oslo, covering the years 1930-1949, with a total of 44,533 deliveries. The total percentage of infant deaths was 5.17; the proportion of infant deaths due to birth injuries, 44 per cent; the total percentage of children discharged alive with evidence of transient or permanent birth injury, 5.08; and the total percentage of birth injuries in surviving and nonsurviving infants, 7.35.

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Vol. 33, Supp. 2, 1954.

Sauramo, Hannes: Histology and Function of the Ovary From the Embryonic Period to the Fertile Age, p. 3.

Sauramo, Hannes: Development, Occurrence, Function and Pathology of the Rete Ovarii, p. 29.

Sauramo, Hannes: Development, Occurrence and Pathology of Aberrant Adrenocortical Tissue in the Region of the Ovary, p. 49.

Sauramo, Hannes: Occurrence, Function and Pathology of Ovarian Sympathicotropic Cells, With Special Reference to Their Differentiation From Interstitial or Hilus Cells, p. 61.

Sauramo, Hannes: Histology and Function of the Ovary During the Fertile Period, With Special Reference to the Effect of Pregnancy, p. 85.

Sauramo, Hannes: Observations on the Histology and Function of the Ovaries in Genital Pathological and General Pathological Cases, With Special Reference to Uterine Myoma, p. 101.

Sauramo, Hannes: The Anatomy, Histology, Histopathology and Function of the Ovarian Vascular System, p. 113.

*Sauramo, Hannes: The Importance of the Utero-ovarian Blood Vessels in Conservative and Operative Gynecology and Obstetrics, p. 127.

Sauramo, Hannes: Some Observations on Ovarian Function, With Special Reference to the Thecal Tissue, the So-called Interstitial Gland, and the Male Part of the Ovary, p. 135.

Sauramo, Hannes: Attempt at an Ontogenetic, Histological and Histopathological Synthesis of the Functions of the Ovary and the Rest of the Reproductive System, p. 143.

Sauramo: Importance of Utero-ovarian Blood Vessels in Gynecology and Obstetrics, Supp. 2.

The entire supplement is written by Hannes Sauramo on the histological, pathological, and functional relationships of the ovaries from the embryonic stage through the fertile period. There is an overabundance of author reference on every page of the text. The chapter dealing with the uteroovarian blood vessels in conservative and operative gynecology is timely. The author describes the course and variations of the ovarian vessels in 80 cases. "The ovarian artery leaves the renal artery on the right in 4 per cent . . . on the left in 10 per cent; in 2 per cent it is given off from the suprarenal artery. The left ovarian vein always opens into the left renal vein. Most commonly the uterine artery gives branches to the uterus, tubes and ovary, and the ovarian artery into the ovary and tube. In 11 per cent the uterine artery does not give off branches to the ovary, and in 20 per cent the ovarian artery does not give off branches to the tube. In 17.5 per cent the ovarian artery is connected only by small anastomosing branches. . . .

"In studying the effect of hysterectomy on both adnexae, it is observed that both ovaries remain practically without arterial branches in 9.5 per cent of all cases and one ovary in 19 per cent. It is probable that hysterectomy occasionally causes disturbances in the nutrition of the ovaries, even though a collateral circulation is established."

JOSEPH J. SMITH, M.D.

American Journal of Surgery

Vol. 87, No. 1, January, 1954.

Pena, Eduardo F.: Prevention of Abortion, p. 95.

Levin, Irving A., and Hertzog, Ambrose J.: Unusual Type of Metastasis for Carcinoma of the Breast With Coincidental Development of Diabetes Insipidus, p. 137.

Vol. 87, No. 2, February, 1954.

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Vol. 87, No. 4, April, 1954.

Fletcher, Wm. E., and Arnold, J. Harold: Carotid Body Tumor. A Review of the Literature and Report of an Unusual Case, p. 617.

*Hardaway, Lt. Col. Robert M., III: Gastroschisis, p. 636.

Hardaway: Gastroschisis, p. 636.

This is the report of a successfully treated case of gastroschisis (a rare congenital malformation in which the abdomen remains open, with viscera protruding), together with a review of the literature on the subject.

A classification of congenital eviscerations is given. These are divided into: (1) omphalocele, (2) intussusception of the ileum through persistent omphalomesenteric duct, and (3) gastroschisis. The author gives an anatomic description of each along with the clinical criteria for making the correct differential diagnosis in cases of congenital evisceration.

The surgical approach to the problem is outlined. It consists briefly of extending the opening of the defect and repositing the bowel within the abdominal cavity. The peritoneum and fascia are not closed and only the skin and subcutaneous tissues are utilized to close the defect in the abdominal wall.

The author outlines the postoperative care and the use of antibiotics in these cases.

A good percentage of these cases of congenital evisceration are today amenable to surgery. Col. Hardaway stresses the following points in considering the survival of those infants coming to surgery: (1) the disproportion between the eviscerated mass and the size of the abdomen, (2) the general condition of the infant, (3) the lack of any other congenital defect, (4) immediate operation, and (5) the use of antibiotics.

Although this condition occurs infrequently, the obstetrician who is cognizant of the fact that surgical correction can be accomplished will be duly rewarded by the survival of an infant in an otherwise hopeless condition.

THOMAS SULLIVAN, M.D.

Vol. 87, No. 5, May, 1954.

Dick, A.: Carcinoma in a Newborn; Report of a Case, p. 673.

*Studdiford, William E., and Decker, Wayne H.: Malignant Manifestations of Papillary Serous Tumors of the Ovary, p. 768.

Studdiford and Decker: Malignant Manifestations of Papillary Serous Tumors of the Ovary, p. 768.

This is a report of three cases of malignant papillary serous tumors of the ovary, in which the authors discuss the gradation of malignancy found in this type of neoplasm.

The main criterion is, of course, the histologic structure. This ranges from well differentiated to highly undifferentiated. With the latter picture there are usually extensive peritoneal metastases. These metastatic lesions are infiltrating and show little or no evidence of degenerative change.

On the other hand, there may be tumors which are histologically well differentiated but which extend beyond the cortex and produce shallow intraperitoneal implants. These metastatic lesions usually show degeneration and calcification.

A third gradation was defined as containing elements from both ends of this table of criteria of malignancy. It included invasion of the stroma by the lining cells and the nature of the metastatic implants.

The authors discuss surgical therapy and speculate on the value of radioactive colloidal gold in the treatment of metastatic lesions in these patients.

THOMAS SULLIVAN, M.D.

Vol. 88, No. 2, August, 1954.

Studdiford, W. E., and Decker, W. H.: Hydatiform Mole, p. 308.

Boletín de la Sociedad de obstetricia y ginecología de Buenos Aires

Vol. 33, No. 468, May 6, 1954.

Bases, Liberto: An Evaluation of 500 Cases of Total Hysterectomy for Leiomyomas, p. 37.

*Bagnati, Enrique P.: Fibrinolytic Action of Menstrual Discharges, p. 44.

Brea, Cesar A., Provenzano, Luis M., Pena, Juan C. Gonzalez: Treatment of Some Pelvic Pains by the Resection of the Superior Hypogastric Plexus, p. 51.

Ahumada, Jorge L., and Ponte, Roberto Rodriguez: Congenital Atresia of the Cervix, p. 56.

Defazio, Francisco: Dysgerminoma of the Ovary, p. 60.

Bagnati: Fibrinolytic Action of Menstrual Discharges, p. 44.

The author undertook to study variations in the enzymatic action of menstrual discharges at different temperatures. Thirteen women hospitalized for minor illnesses of nongynecologic origin were used as subjects; all had entirely normal gynecologic histories and physical findings. The ages of the patients varied between 19 and 38 years. Menstrual fluid was collected by means of metallic suction curette; in no case was it necessary to perform preliminary dilation of the cervix. In this way, no nonmenstrual blood was included in the specimen. The cannula was left in place for at least one hour, during which time each patient produced for study some 3 to 4 c.c. of a syrupy, dark-red fluid with a characteristic odor, entirely without evidence of blood clot, and perfectly free from admixture with cervical or vaginal secretions, having been collected directly from high up inside the uterus. The menstrual fluid was then centrifuged, and the supernatant liquid (termed "menstrual serum") was siphoned off and used for the experiments. Serum obtained from citrated peripheral blood was used for comparison. Various mixtures of "menstrual" and "physiological" serum with calcium chloride added were then incubated, and the results read at 24 and 48 hours.

The experiments showed that menstrual discharge possesses a definite fibrinolytic activity, the intensity of which varies within narrow limits. The author tentatively concludes the menstrual fluid contains a lytic substance which has a specific action on the clotting mechanisms of peripheral blood. If fluidity of the menstrual discharges is predicated to be on the basis of proteolytic action, it seems logical to assume that the demonstrated enzyme represents an important feature of the etiology of menstruation. A given amount of menstrual serum varies in its lytic activity depending on certain other factors. For example, at 57° C. all lytic activity is abrogated, whereas incubation at 37° C. favors fibrinolysis. This fibrinolytic activity at 37° C. is slightly more marked than that at room temperature, although this difference is very slight in some of the patients studied. A mixture of menstrual serum, normal citrated plasma, and calcium chloride solution always produced clotting, while mixtures of menstrual serum and calcium chloride without normal plasma demonstrated no clotting activity whatsoever.

DOUGLAS M. HAYNES, M.D.

The Journal of Obstetrics and Gynaecology of the British Empire

Vol. LXI, No. 1, February, 1954.

Walker, C. H. M., and Balf, C. L.: Capillary Resistance Studies
Part I: The Newborn Infant, p. 1.
Part II: Late Pregnancy, Labour and Early Puerperium, p. 17.

Dunster, Marjorie O., McGowan, G. K., and Bennett, Douglas: The Effect of Cation Exchange Resins in the Treatment of Pre-eclamptic Toxaemia of Pregnancy, p. 31.

*Way, Stanley: The Aetiology of Carcinoma of the Body of the Uterus, p. 46.

*Carey, H. M.: An Improved Technique for the Induction of Labour, p. 59.

Bride, John Webster: Some Manchester Pioneers in Obstetrics and Gynaecology, p. 69.

Martin, R. T.: Adenocarcinoma of the Vaginal Vault Following Gestational Hypertrophy of the Cervix Uteri, p. 81.

Nicol, T., and Snell, R. S.: The Appearances of Lipoid in the Cells of the Vaginal Smear of the Guinea-Pig, p. 85.

*Wendell-Smith, C. P.: The Lower Uterine Segment, p. 87.

*Digby, I. F.: A Case of Quintuplet Pregnancy, p. 94.

Faris, I. B., and Kahlenberg, B.: Intravenous Pitocin by the Drip Method in the Induction of Labour, p. 96.

Davis, L. R., and Jennison, R. F.: Response of the "Physiological Anaemia" of Pregnancy to Iron Therapy, p. 103.

MacKinnon, I. L.: Observations on the Pulse Rate During the Human Menstrual Cycle, p. 109.

Chaudhuri, M.: Perforated Uterus Complicated by Vaginal Prolapse and Strangulation of the Intestine. A Report of Two Cases, p. 113.

Murless, Bryan G.: Foetal Head Extractors and Lower Uterine Section, p. 116.

Bromberg, Yehuda M., and Rozin, Samuel: Pregnancies in a Case of Endometrial Tuberculosis Treated by Streptomycin, p. 121.

Way: Aetiology of Carcinoma of Body of Uterus, p. 46.

Many individuals believe that there is an increased incidence of diabetes, uterine polyposis, endometrial hyperplasia, feminizing tumors, fibroids, obesity, and late menopause in patients with carcinoma of the uterine fundus. There is also apparently an inherited predisposition to this form of female genital cancer. The author calls upon his extensive experience with this disease and combines his statistics with many quoted from the literature to show the likelihood of a single etiological factor being responsible for all these diverse conditions. A number of interesting cases are cited and the single factor which could apparently explain the more than coincidental occurrence of these apparently unrelated diseases is an overactivity of the anterior pituitary. It is concluded that not all of the manifestations of anterior pituitary overactivity may be seen in the same patient, thus explaining how one individual may develop fibroids, another diabetes or carcinoma of the uterus, while another may develop all or a combination of these diseases. The author suggests that the tendency to overactivity of the anterior pituitary may be the one factor which is inherited.

STEWART A. FISH, M.D.

Carey: Improved Technique for Induction of Labour, p. 59.

The author describes an ingenious method for the recording of intrauterine amniotic-fluid pressure during labor. Using an S-shaped stylette, the membranes are punctured high up. With a special introducer, a polyethylene tube is inserted into the amniotic cavity, and the free end of the tube is attached to a manometer. To prevent amnionitis, a solution of penicillin and streptomycin is fed into the amniotic sac through this tube when pressure readings are not being made. The author's technique for induction of labor involves primary rupture of the membranes and the use of intravenous Pitocin by infusion when necessary to initiate or augment uterine contractions. Five international units of Pitocin are dissolved in a liter of glucose and water and the infusion started at the rate of 5 to 8 drops per minute. Since simultaneous recordings of intrauterine pressure are made through the polyethylene tube within the amniotic sac, the efficacy of the uterine contractions may be graphically demonstrated and overdosage of Pitocin with resultant tonic contractions avoided. A number of representative cases are discussed and the records of uterine activity throughout labor are shown. It is noted that the small volume of antibiotic solution run into the amniotic cavity has no effect on the recordings of uterine tone or activity. Likewise, the leakage of a small amount of fluid from the amniotic cavity after the initial loss with rupture of the membranes, is without further discernible effect on uterine activity. This is

probably due to the adaptation process which any hollow viscus undergoes, allowing it to adjust its capacity to the volume of its contents. The author has frequently used the technique of induction just described in patients with severe toxemia of pregnancy who do not respond to medical therapy, in an effort to reduce the incidence of abdominal deliveries.

STEWART A. FISH, M.D.

Wendell-Smith: Lower Uterine Segment, p. 87.

The author presents a detailed gross and microscopic study of the lower uterine segment. The musculature and mucosal structure of the nonpregnant uterus are described. A good schematic representation of some of the changes which occur in the lower uterine segment during pregnancy is given. The attenuation of the lower uterine segment during labor is shown to be the result of a differential movement of muscle layers and bundles as a result of stress. The changes which occur in obstructed labor are also demonstrated. This is a well-documented and complete anatomic study of the lower uterine segment.

STEWART A. FISH, M.D.

Digby: Case of Quintuplet Pregnancy, p. 94.

This is the first reported case of a quintuplet pregnancy occurring in the British Isles. Seventy-four cases of quintuplet pregnancy have been reported in the world literature in the past two centuries. Only two sets of quintuplets have survived, namely, the Dionnes of Canada and the Diligentis of Argentina. In this instance, the patient was a 35-year-old para iv, gravida v, who had four previously normal pregnancies. In this pregnancy the patient developed leg edema, headache, and malaise in the thirtieth week of gestation. She was admitted to the hospital at this time, and hydramnios was diagnosed. There was an associated hypertension and albuminuria. X-ray of the abdomen revealed quintuplets, one fetus presenting by breech and four by vertex. She was treated with bed rest and sedatives and no fetal heartbeats or fetal movements were ever discovered. While in the hospital the patient went into spontaneous labor and delivered five stillborn male infants. The placenta separated uneventfully and there was no postpartum hemorrhage. The infants all weighed between 2 pounds, 8 ounces, and 3 pounds, with a total weight of 15 pounds, 12 ounces. The placenta weighed 2 pounds. There are two photographs, one of the antepartum x-ray of the abdomen and one of the placenta, showing five cords arising from this structure. The literature is cited only briefly and there is a brief comment on the pregnancy.

STEWART A. FISH, M.D.

Vol. LXI, No. 3, June, 1954.

*Bailey, K. Vernon: A Clinical Investigation Into Uterine Prolapse With Stress Incontinence. Treatment by Modified Manchester Colporrhaphy. Part I, p. 291.

*White, Thomas G.: Deflexion Attitudes of the Foetus in Utero With Special Reference to the Aetiology and Diagnosis of Face and Brow Presentation, p. 302.

Stewart, D. B., and Bernard, R. M.: A Clinical Classification of Difficult Labour and Some Examples of Its Use, p. 318.

Buckell, E. W. C., and Owen, T. K.: Chorionepithelioma in Mother and Infant, p. 329.

Law, R. G.: Prolonged Labour in Multiparae, p. 331.

Morris, W. I. C.: The Management of Eclampsia, p. 339.

Macafee, C. H. G.: Endometriosis of Episiotomy Scar, p. 349.

Berenbaum, Morris, C., and Korn, Gerald W.: Tubal Pregnancy in Tuberculous Salpingitis. Report of a Case With Histochemical Analysis of Crystalline Inclusions, p. 351.

Russell, J. K.: Primary Infertility Affecting Three Brothers and One Sister, p. 354.

Winston, R. M.: The Design of Male Amphibian Pregnancy Tests. Application to Bufo Regularis Reuss, p. 356.

Clemetson, C. A. B., and Churchman, J.: The Placental Transfer of Amino-Acids in Normal and Toxaemic Pregnancy, p. 364.

*Millar, W. Gordon: Investigation and Treatment of Female Genital Tuberculosis, p. 372.

Ward, O. Conor: Ventricular Haemorrhage in the Newborn, p. 380.

*Harston, Antony P. B.: Mitral Valvotomy in Pregnancy With Two Illustrative Cases, p. 382.

Myles, T. J. M.: Primary Abdominal Pregnancy. Case Report, p. 387.

MacKinnon, Pamela C. B.: Variations in the Number of Active Palmar Digital Sweat Glands During the Human Menstrual Cycle, p. 390.

Bailey: Clinical Investigation Into Uterine Prolapse With Stress Incontinence. Part I, p. 291.

In an effort to determine the effectiveness of the Manchester colporrhaphy in the treatment of stress incontinence in patients with prolapse, the author has reviewed 209 cases personally operated upon. An effort was also made to determine by cystourethrography the actual anatomic changes occurring at the bladder neck and along the course of the urethra before and after operation. Of the 209 cases reviewed, in 83 there was stress incontinence in addition to the prolapse. In all cases the prolapse was cured by the Manchester colporrhaphy, but of the 83 with stress incontinence there were 51 failures. Of the 32 cures, 29 patients had restoration of the posterior urethrovesical angle as demonstrated by cystourethrography and, of the 51 failures, 44 showed abnormal x-rays, indicating that restoration of this angle is important in determining the success or failure of the procedure. The author has modified the classic Manchester colporrhaphy in an attempt to increase the cure rate in patients with prolapse and stress incontinence, and his technique is described in detail. This modification is essentially a colporrhaphy including a suburethral bolster followed by a suprapubic paraurethral suspension similar in many ways to that employed by Marshall and Marchetti. This combined technique restores the posterior urethrovesical angle accurately in almost every instance. Of 35 cases recently treated by this method, 32 had complete anatomic and symptomatic cures. This modified colporrhaphy is indicated in about one-third of the patients with prolapse who complain of stress incontinence, or in about 13 per cent of all cases. The combined operation is selected as the procedure of choice in patients who demonstrate by x-ray a marked degree of downward rotational descent of the upper urethra and a loss of the posterior urethrovesical angle. When these two findings are noted on cystourethrography, the operation may be elected as an initial procedure. The author emphasizes the fact that colporrhaphy must remain the basis of all operations performed for stress incontinence in patients with prolapse, since without it the results are temporary due to the constant dragging effect of the prolapsed uterus and anterior vaginal wall. The anatomy of the bladder neck and the structures involved in the colporrhaphy operation are considered in detail.

STEWART A. FISH, M.D.

White: Deflexion Attitudes of the Foetus in Utero With Special Reference to Aetiology and Diagnosis of Face and Brow Presentation, p. 302.

Existing pertinent literature on the etiology of brow and face presentation is reviewed and the author shows there is no acceptable evidence that contracted pelvis, disproportion, coils of umbilical cord around the neck or posterior positions of the occiput cause face or brow presentation. The true cause of these deflexion attitudes of the fetus, as suggested by the author, is increased extensor tone in the muscles of the back and neck of the fetus. The cause of this increased extensor tone is not known. Since it occurs in breech and transverse presentations frequently, however, it is thought to be an intrinsic fetal condition. The author stresses the difficulty of diagnosing deflexion attitudes of the fetus by abdominal palpation and he believes that primary deflexion attitudes are much more common than present studies indicate. The increased incidence of face and brow presentation in

multiparas and in individuals with placenta previa or hydramnios is explained by the fact that the head does not descend into the pelvis and become fixed in these conditions before the onset of labor, allowing the fetal head to extend. It is difficult to demonstrate increased extensor tone in the newborn because of the difficulty in overcoming the forces of gravity once the infant is no longer in the liquid medium of the amniotic cavity. Five cases of primary face presentation are reported and the author believes that if routine x-ray studies of the fetus in utero were made, a large number of deflexion attitudes of the fetal head would be discovered. This paper was awarded the Katherine Bishop Harman Prize of the British Medical Association in 1953.

STEWART A. FISH, M.D.

Millar: Investigation and Treatment of Female Genital Tuberculosis, p. 372.

The author reports 36 cases of histologically proved tuberculous endometritis. Diagnosis was made by curettage and guinea pig inoculations. Difficulties involved in establishing a diagnosis by these two methods are discussed. Abdominal pain was the presenting symptom in one-third of the cases and the most frequent menstrual disorder was menorrhagia. Extragenital tuberculous lesions were present in 26 patients, of which 11 were pulmonary and 5 abdominal. Of the 29 married patients, 25 were nulliparous. Of 22 cases in which tubal insufflation was performed, tubal blockage was present in 19. The human strain of tuberculosis was cultured in 27 patients and no bovine tuberculosis was discovered. An attempt was made to culture menstrual fluid and was totally unsatisfactory. Treatment consisted of 1 Gm. of streptomycin sulfate and 15 to 20 Gm. of para-aminosalicylic acid daily for 90 days. Patients who failed to respond to this treatment or developed recurrences were given Isoniazid, 200 mg. daily for 8 weeks. After a year or longer, 29 patients (80.5 per cent) showed no evidence of pelvic tuberculosis while 7 (19.5 per cent) showed evidence of residual disease. Three of the patients with persistent tuberculosis have been followed one year after Isoniazid therapy and tests in one remained positive. It is too early to evaluate the results of Isoniazid therapy in the other patients reported. Tubal patency was investigated again after therapy and patency had developed in three cases in which the tubes were apparently blocked before therapy. These findings suggest that provided the tubal involvement is not massive, there is a distinct possibility that recanalization may take place after some years. Future pregnancies should be possible but so far in this series no pregnancies have occurred. There were four instances of generalized dermatitis from the streptomycin and one case in which vestibular function was impaired. There were no complications associated with Isoniazid therapy.

STEWART A. FISH, M.D.

Harston: Mitral Valvotomy in Pregnancy, p. 382.

Two pregnant patients with marked mitral stenosis are reported. Mitral valvotomy was performed on both patients at about 24 weeks' gestation. Marked symptomatic and functional improvement was noted. Both patients subsequently had normal vaginal deliveries and have continued to do well.

The indications for mitral valvotomy in pregnancy are listed and the risks of the procedure enumerated. The author stresses the importance of careful selection of patients and the need for close cooperation between the obstetrician-gynecologist, cardiologist, and thoracic surgeon in the management of this problem.

STEWART A. FISH, M.D.

Correspondence

Dammerschlaf and Demerol

To the Editors:

Re: Dammerschlaf (Twilight Sleep)

Under the false headline "Pudendal Block Anesthesia in Obstetrics" (vol. 68, pp. 969-973, 1954), your author describes a twilight sleep with supplementary local anesthesia. He has fallen for the manufacturer's trick linking *DEMEROL* to *DAMMER*schlaf by its very sound.

The original German twilight sleep of two generations ago was induced by a combination of scopolamine and morphine, potentiating their soporific and analgesic qualities, while counteracting each other's toxicity.

Demerol simply adds to the toxicity of scopolamine, as they both belong chemically to the same family, but it is inferior to morphine in soporific and analgesic effects.

If your author had honestly returned to the German formula which I have sucessfully used for the last 30 years, he would have needed NO local anesthesia at all.

ALFRED ROSSKAMM ROSS, M.D., L.R.C.S.

BELFAST, NEW YORK
JAN. 20, 1955

Reply by Dr. Harris

To the Editors:

I am very glad to be allowed to explain my position, for there is obviously a misinterpretation of my intent.

As stated in the title of my article, "Pudendal Block Anesthesia in Obstetrics," I was explaining to our local society my experiences with a simple type of anesthesia—*not analgesia.* In the body of the article I did make the following statement about the use of analgesic agents:

"It is not the purpose of this paper to review long lists of drugs which have been used to relieve pain and distress during labor. . . . From a broad viewpoint then, modern obstetric analgesia leaves little to be desired. . . ."

This statement was meant to be all inclusive, and certainly would not exclude "Dammerschlaf" (twilight sleep). I am quite confident that the original German formula must possess many virtues, as evidenced by a strong exponent after these many years of experience. However, I am, as stated, happy with the combination that I use at present, but have an open mind on the subject and am quite willing to change when I am convinced that it is for the benefit of my patients. So it is not a matter of "honesty," but rather one of preference. I can assure you that I did not confuse "Dammerschlaf" with "Demerol" although there is a slight phonic similarity.

My series is now well over one thousand cases and I am more enthusiastic than ever.

1211 AVENUE O

LUBBOCK, TEXAS
MARCH 7, 1955

Adenosis of the Vagina

To the Editors:

I read with a great deal of interest the article, "Myxometra Resulting From Mucous Metaplasia of the Endometrium," by Drs. Cyril Solomon and Wolfe Polishuk, in the December, 1954, issue of the JOURNAL.

My comments stem from an interest in the abnormal development and differentiation of Müllerian epithelium. I am presently completing a paper and case report on adenosis of the vagina and its relationship to primary mucinous adenocarcinoma of the vagina. The desire for an adequate period of follow-up has delayed submitting the paper for publication. There are many similar features between a case observed by Dr. A. A. Simkus* and me and the one reported by Solomon and Polishuk and in order to bring them out it will be necessary to touch briefly upon the clinical entity termed by Plaut[1] adenosis of the vagina.

The human vagina is normally devoid of glands, and when glandular structures are detected in the vaginal wall they so resemble cervical glands that they are spoken of as aberrant or ectopic cervical glands. There is strong evidence that these abnormally located mucous glands owe their origin to an embryological flaw in the development of the vagina. From various reliable sources[2, 3, 4] it is generally accepted that the permanent lining of the vagina is derived from the epithelium of the urogenital sinus and not from the Müllerian epithelium. In the upward growth of the urogenital sinus epithelium, the lateral wall of the vaginal cleft is first occupied, while in the upper midline a tongue of Müllerian epithelium lags and remains for a longer period of time before being replaced by the epithelium of the urogenital sinus. It is conceivable that, in the event of a developmental flaw, Müllerian epithelium may remain and at a later date have the ability to differentiate into mucin-secreting glands as it normally does in the cervix uteri. Such a chain of events could explain the presence of glands in the vaginal wall more logically than the terms ectopic or aberrant cervical glands. Unlike cervical glands, these glands do not show branching or communicate with the vaginal lumen except as a complication, as there are no ducts associated with the glands. The mucin secreted by these glands may by sheer mechanical force fracture, or by its very irritating nature macerate, the normal overlying vaginal epithelium and come to communicate with the vaginal canal, producing a copious, irritating, and typical mucoid discharge. The gross appearance of the complicated lesion is generally typical. Where the mucin has eroded the vaginal epithelium there is a red, granular surface formed by secreting glands that completely replace the normal epithelium. Microscopically the glands are made up of secreting columnar epithelium in single layers.

Normally the Müllerian epithelium differentiates into epithelial structures typical of the Fallopian tubes, the endometrium, and the cervix. It seems quite reasonable that Müllerian epithelium in a process of abnormal differentiation can be responsible for the development of mucinous glands above the endocervix in any structure derived from Müllerian epithelium. In the gross and microscopic description of Solomon and Polishuk's case it appears that the same process of complication occurred as is seen in adenosis of the vagina. The abnormally located mucinous glands through fracture or maceration of the overlying endometrial epithelium made it possible for the mucous discharge to communicate with the uterine and vaginal cavities. The lack of symptoms during the patient's childbearing period is also typical in the majority of the cases of vaginal adenosis. It merely indicates that the abnormal glands did not develop until later in life or if present they were not involved in the complication of eroding the confining endometrium and were thereby asymptomatic. I think this explanation would be more acceptable than the unsatisfactory terms of "widespread dissemination [of mucous glands] from the endocervix . . . or . . . metaplasia of an uncommon type."

A further point of interest is that a similar but more extensive case was reported by Drs. H. W. Neidhardt and J. T. Downs,[5] where the entire uterus, cervix, and parametrium showed innumerable mucus-secreting glands. The case was reported as a rare

*Dr. Simkus is a resident in the Department of Obstetrics and Gynecology, Shreveport Charity Hospital, Shreveport, La.

invasive lesion of the uterus by mucinous glands and of obscure origin. In both cases it would have been interesting if a vaginal biopsy had been obtained to determine if the process had extended down to involve the vagina. Involvement of the vaginal wall, of course, would not necessarily be expected since the abnormality probably occurs differently in each case. In adenosis of the vagina there is retention of Müllerian epithelium with differentiation at a later date into mucin-secreting epithelium. In Solomon and Polishuk's case there is probably a flaw in the differentiation of Müllerian epithelium in the uterus proper. The endometrial epithelium, as it does normally, probably sent down buds of cells that formed the normal endometrial glands, while portions of this same epithelium differentiated in the direction of mucin-secreting or cervical-type glands. Such a process would not intimate an invasive nature for cervical glands.

HARRY MARX TRIFON, M.D.

772 SUTTER AVENUE
PALO ALTO, CALIFORNIA
JAN. 15, 1955

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5. Neidhardt, H. W., and Downs, J. T., III: AM. J. OBST. & GYNEC. 58: 703, 1949.

Reply by Dr. Solomon

To the Editors:

I want to thank Dr. Trifon for his interesting comment on the paper written by Dr. Polishuk and myself.

We were familiar with the paper of Drs. Neidhardt and Downs which resembled ours in having mucus-secreting glands in the endometrium and myometrium. Our case differed, however, in its filling the uterus with mucus, which did not occur in their case. Drs. Neidhardt and Downs could not rule out adenocarcinoma of the mucous glands of the endocervix nor, frankly, can we, since later spread to the parametrium was found.

Perhaps we should have, in our speculations, included the statement that "congenital origin could not be ruled out."

CYRIL SOLOMON, M.D.

FRENCH HOSPITAL
330 WEST 30TH STREET
NEW YORK 1, N. Y.
MARCH 11, 1955

Item

Comité International de Liaison des Organismes Professionnels de Gynécologues et Obstétriciens

The Second Meeting of the International Association of Gynecologists and Obstetricians will commence on Monday, June 27, 1955, at the Hôtel des Syndicats Médicaux Français, 60, boulevard de Latour-Maubourg, Paris VIIe. All communications relating to this meeting are to be addressed to Dr. Jacques Courtois, Secrétaire Général, 1, Rue Racine, Saint-Germain-En-Laye (S.-&-O.)

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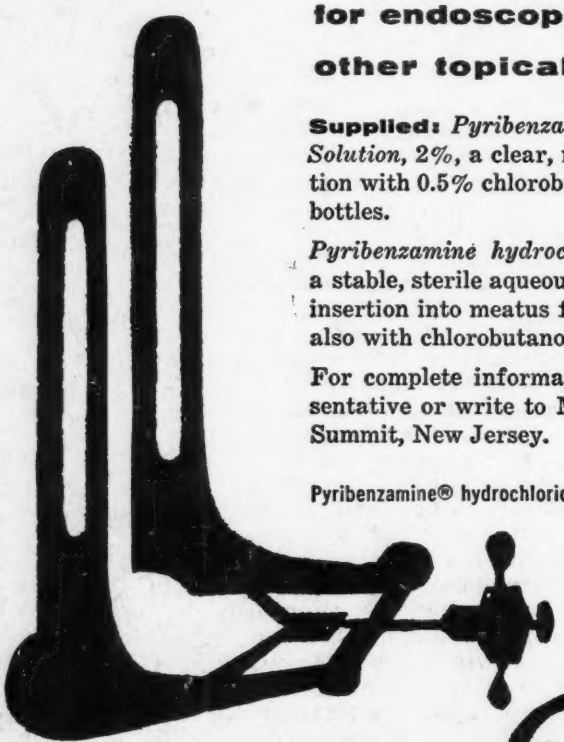

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